THE NATIONAL CLEARINGHOUSE FOR MENTAL HEALTH INFORMATION

VOL. 10 NO. 4 - April 1971

PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results. For information or correspondence with the National Institute of Mental Health concerning Psychopharmacology Abstracts, changes of address, or removal of names from the mailing list see the inside back cover page.

Use of funds for printing this publication approved by the Director of the Office of Management and Budget, September 1, 1970.

01 CHEMICAL SYNTHESIS. ISOLATION AND CHARACTERIZATION

64090
AUTHORS: Villeneuve, A.
ADDRESS: Division de Recherches, Hospital St-Michel-Archange, Quebec, Canada
TRTITLE: /Classification, nosology, and rating scales of psychotropic drugs./
TITLE: Classification des medicaments psychotropes, nosologie et echelles d'appreciation.
SOURCE: Canadian Psychiatric Association Journal (Ottawa).
SOURCEID: 15(2):205-213, 1970.

Various classifications of psychotropic drugs are currently in use. Generally, psychotropic drugs are first classified according to their clinical action, and then divided into subgroups according to their distinctive chemical structure. Depending upon the country, there are different classifications of mental illness which do not always correspond to one another. For several years, efforts have been made to standardize these classifications in order to facilitate comparisons of diagnoses on an international level. Transcultural studies have been undertaken in recent years in the field of nosology by means of rating scales. Rating scales are also used in psychopharmacology to assess the change in the mental state during clinical trials. Some of them can be applied to most psychotic states, while others are limited in scope to one nosological entity or to one symptom. Stereotyped profiles, an empiric typology and profiles of drug responders have been derived from some rating scales. The data obtained from these scales and submitted to elaborate statistical analyses are directly dependent upon the accuracy of the clinical assessment. No deduction, statistical or other, based upon these scales, will yield valid results if the clinical assessment is deficient. 38 references. (author abstract modified)

64159
AUTHORS: Fontani, Febo; Morandini, Franco.
ADDRESS: Control Department of RECORDATI s.a.s., Milan, Italy
TITLE: Colorimetric determination of amphetamine salts in dosage forms.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(6):411-413, 1970.

A colorimetric method for the determination of primary amines has been applied to the assay of amphetamine salts in dosage forms. Aqueous solutions of amphetamine salts, heated in acidic medium with 0.5% 2,5-dimethoxytetrahydrofuran and subsequently reacted with a 2%solution of p-(dimethylamino)benzaldehyde in an 85 to 15 mixture of glacial acetic acid and hydrochloric acid, give a red color. This reaction was found useful for photometric determinations at 577 nm. The following compounds, sometimes associated with amphetamine in dosage forms, gave no interference in the assay: dimenhydrinate, diphenhydramine hydrochloride, phenylephrine hydrochloride, methamphetamine hydrochloride, adrenaline bitartrate, diphenylhydantoin, and mephobarbital. Imidazole, purine derivatives, and secondary and tertiary amines do not undergo the reaction and do not interfere. Primary aliphatic and aromatic amines, including amino acids, do interfere. 9 references. (author abstract modified)

64258
AUTHORS: Saenz, Reynaldo V.; Brown, Robert G.; Isaacson, E. I.; Delgado, Jaime N.
ADDRESS: School of Pharmacy, Northeast Louisiana State College, Monroe, Louisiana 71201
TITLE: Synthesis of some glycidic hydrazides and amides as potential psychotropic agents and anticholinergic agents.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(7):942-947, 1970.

Some glycidic hydrazides and amides were synthesized by hydrazinolysis or aminolysis of glycidic esters as potential psychotropic agents and anticholinergic agents. The hydrazides thus obtained were subjected to suitable acylating or alkylating reagents to obtain N -substituted hydrazides. The results of a preliminary pharmacological evaluation are summarized. The synthesized compounds were tested for their ability to reverse reserpine hypothermia in mice. Compounds synthesized as potential anticholinergics were evaluated for their spasmolytic activity using isolated rabbit ileum. 12 references. (author abstract modified)

64264
AUTHORS: Murty, B. S. R.; Baxter, R. M.
ADDRESS: Faculty of Pharmacy, University of Toronto, Toronto 181, Canada
TITLE: New compounds: structural analogs related to asarone and mescaline.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(7):1042-1043, 1970.

The synthesis and spectral data of a series of trimethoxyphenyl derivatives related to asarone and mescaline are reported. The physical and spectral data were obtained by means of thin layer chromatography, UV and NMR spectra. The data is presented in a comprehensive chart. 6 references. (author abstract modified)

63634
AUTHORS: Keiper, Ronald R.
ADDRESS: Department of Biology, Pennsylvania State University, Mont Alto, Pennsylvania 17237
TITLE: Studies of stereotypy function in the canary (Serinus canarius).
SOURCE: Animal Behaviour (London).
SOURCEID: 18(2):353-357, 1970.

Caged canaries exhibit 2 general repetitive stereotypies, route tracing and spot picking. Experiments were conducted to determine the influence of certain environmental and physiological factors upon these avian stereotypies. Stereotypies were counted in 5 min observation periods excluding time spent singing, feeding, drinking, or preening. Twelve of these 5 min periods made up an experimental test series. Presentation of both novel stimuli (plastic beads and a mirror) and social stimuli (brief daily view of a bird in an adjacent cage) significantly reduced both canary stereotypies, apparently by initiating other incompatible behaviors. By administering hormones or hormone analogues, which initiate reproductive behavior and moulting, alternate behaviors were activated which significantly reduced the number of route traces. These results suggest that in caged canaries, stereotypies occur primarily to supply the birds with a source of stimulation. 15 references. (Author abstract modified)

63798
AUTHORS: Smits, S. E.; Takemori, A. E.
ADDRESS: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46206
TITLE: Quantitative studies on the antagonism by naloxone of some narcotic and narcotic-antagonist analgesics.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 39(3):627-638, 1970.

Naloxone was used to study the antagonism of the analgesic effects of some narcotics (morphine sulphate, levorphanol tartrate, and methadone hydrochloride) and narcotic antagonists (pentazocine, cyclazocine, and nalorphine hydrochloride). The analgesic assay used was the mouse phenylbenzoquinone stretching test. The in vivo equivalent of a pA2 value (apparent pA2) for naloxone was determined with each agonist. These values were found to be significantly larger with the narcotics than with the narcotic antagonists. The slopes in the apparent pA2 plots were also found to be significantly different. It was concluded that the difference in slopes was probably not due to a lack of equilibrium in one of the two groups of analgesics. The results suggest that the narcotic and the narcotic - antagonist analgesics may inhibit stretching in this assay by interacting either with two different receptors or with the same receptor in a different manner. 31 references. (author abstract)

63825
AUTHORS: Wurtman, R. J.; Rose, C. M.; Matthysse, S.; Stephenson, J.; Baldessarini, R.
ADDRESS: Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139
TITLE: L-dihydroxyphenylalanine: effect on S-adenosylmethionine in brain.
SOURCE: Science.
SOURCEID: 169(3943):395-397, 1970.

L-dopa administered to 45 adult male rats in a single i.p. dose (100mg/kg) resulted in reduction of brain S-adenosylmethionine (SAMe) to 76% that of normal after 45 minutes. The adrenal medulla content of SAMe was decreased by 51%, after administration of L-dopa 10mg/kg; a much larger dose of 100mg/kg did not significantly depress concentration of SAMe in the liver during this time interval. Concentration of SAMe in the brain varied diurnally in the rats

tested; L-dopa lowered this concentration whether administered at the daily peak or at the nadir. 19 references.

63888
AUTHORS: Henning, M.; Rubenson, A.
ADDRESS: Department of Pharmacology, University of Goteborg S-400 33, Goteborg 33, Sweden
TITLE: Central hypotensive effect of L-3,4-dihydroxyphenylalanine in the rat.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(8):553-560, 1970.

The influence of L-dopa on blood pressure in conscious rats before and after pretreatment with alpha-hydrazino-alpha-methyl-beta-(3,4-dihydroxyphenyl)propionic acid (MK 485), a decarboxylase inhibitor with minimal central actions was studied. Mean arterial blood pressure was recorded through indwelling arterial catheters in conscious normotensive Sprague-Dawley rats.
L-3,4-Dihydroxyphenylalanine (L-dopa) was given in various doses intraperitoneally, alone and after pretreatment with an inhibitor of dopa decarboxylase, MK 485 or seryl-2,3,4-trihydroxybenzyhydrazine (Ro 4-4602). L-Dopa (50mg/kg) produced a hypertensive response which was abolished by MK 485 (100mg/kg). A larger dose of L-dopa (200mg/kg) after MK 485 caused a significant lowering of blood pressure after 15 to 20 min. After Ro 4-4602 (400 plus 200mg/kg), injection of L-dopa (200mg/kg) had no significant effect on blood pressure. The hypotensive response to L-dopa (200mg/kg) after MK 485 was not influenced by the central dopamine receptor blocking agent, spiroperidol (0.1mg/kg), but could be completely inhibited by the dopamine beta-hydroxylase inhibitor, bis-(4-methyl-1-homopiperazinyl-thiocarbonyl)disulphide (FLA 63) (40mg/kg). Pretreatment with protriptyline (10mg/kg) completely blocked the hypotensive effect of L-dopa after MK 485. In correlative biochemical experiments, levels of noradrenaline and dopamine were determined in brain, heart and femoral muscle. L-Dopa (200mg/kg) alone caused a significant increase of dopamine levels in all tissues. After MK 485 and Ro 4-4602 L-dopa did not significantly increase the levels of dopamine in heart or femoral muscle; however, brain dopamine levels were increased more than after L-dopa alone, but brain dopamine levels after Ro 4-4602 were significantly lower than after MK 485, indicating some central decarboxylase inhibition by Ro 4-4602. L-Dopa alone reduced the noradrenaline content of the heart and this effect was prevented by MK 485 and Ro 4-4602. The results show that decarboxylation of L-dopa in both the central and the peripheral nervous system leads to an increase in blood pressure. Decarboxylation of L-dopa in the central nervous system only results in a hypotensive response, provided that high amounts of dopamine are formed in the brain. This effect was prevented by an inhibitor of dopamine beta-hydroxylase but not by a dopamine receptor blocker. Therefore, a central noradrenaline mechanism seems to be involved. The presence of an intact membrane pump in noradrenaline neurons may be essential since protriptyline also blocked the hypotensive action. 34 references. (author abstract modified)

63980
AUTHORS: Stevenson, I. H.; Turnbull, M. J.
ADDRESS: Department of Pharmacology and Therapeutics, University of Dundee, Dundee, Scotland
TITLE: The sensitivity of the brain to barbiturate during chronic administration and withdrawal of barbitone sodium in the rat.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 39(2):325-333, 1970.

The sensitivity of the central nervous system to barbiturate was determined in rats during the chronic administration of barbitone sodium and after its withdrawal. Rats received barbitone sodium (100mg/kg daily), increased at weekly intervals by 100mg/kg until the daily dosage was 400mg/kg. It was found that the brain barbiturate

concentration determined on awakening from a hypnotic dose administered intraperitoneally was found to increase throughout the period of barbitone administration. A similar gradual development of central nervous system tolerance was indicated by measuring the duration of anesthesia following an intraventricular injection of pentobarbitone (500mcg in 20 microliter). The change in sensitivity of the brain which occurred during the period of barbitone administration was not demonstrable from the measurement of sleeping time following intraperitoneal injection of barbitone or pentobarbitone. After withdrawal, the sensitivity of the brain to barbiturate gradually returned to normal. It was concluded that the hypersensitivity to pentobarbitone, but not to barbitone, which develops after withdrawal of barbitone sodium is due to a decreased drug metabolizing capacity. 8 references. (author abstract modified)

63981
AUTHORS: Singh, K. P.; Sharma, V. N.
ADDRESS: Department of Pharmacology and Experimental Therapeutics, B.N.T. Medical College, Udaipur, India
TITLE: Chemical constitution and drug action of N-substituted phenothiazine in ventricular ectopic tachycardia.
SOURCE: Japanese Journal of Pharmacology (Kyoto).
SOURCEID: 20(2):173-178, 1970.

10-N substituted phenothiazine derivatives were examined in ventricular ectopic tachycardia and their structural features responsible for antiarrhythmic activity elicited. The phenothiazines included chlorpromazine, 10-propyl phenothiazine, 10-isopropyl phenothiazine, 10-tertiary butyl phenothiazine, 10-butyl phenothiazine, 10-cyclopentyl phenothiazine, prothipendyl, methoxypromazine, levomepromazine, 4595 R.P. and multergan. Dogs were the experimental subjects. It was found that a 4 carbon atom straight side chain is possibly responsible for maximum activity. A 4 carbon atom branched chain, although quite active, is less active than compounds with 4 carbon atom in a straight side chain. A 3 carbon atom branched chain is more active than the 3 carbon atom straight chain. A 5 carbon atom cyclic ring reduces the activity of the compound. The compounds possessing no substitution at position 2 are more active. Next in order of potency are those which have OCH3 or Cl group at position 2. Among amino derivatives compounds possessing B-methyl group in the side chain are more active, the presence of a pentavalent nitrogen atom possessing sulphonyl methyl group in the molecule decreases activity to a marked extent. 11 references. (author abstract modified)

63982
AUTHORS: Kato, Ryuichi; Onoda, Kinichi; Sasajima, Michitada.
ADDRESS: Department of Pharmacology, National Institute of Hygienic Sciences, Setagaya-ku, Tokyo, Japan
TITLE: Effects of morphine treatment and starvation on the substrate interaction with P-450 in the oxidation of drugs by liver microsomes.
SOURCE: Japanese Journal of Pharmacology (Kyoto).
SOURCEID: 20(2):194-209, 1970.

This study was done to determine whether the decrease in the hexobarbital hydroxylation and aminopyrine N-methylation in liver microsomes from morphine treated and fasted male rats is related to an impairment of androgen induced stimulation of the substrate-P-450 interaction. The administration of morphine to male rats markedly decreased the magnitude of spectral change induced by hexobarbital and aminopyrine in liver microsomes. The decrease in the binding capacity of cytochrome P-450 for hexobarbital and aminopyrine was assumed to be a responsible factor. With aniline and zoxazolamine the binding capacity of cytochrome P-450 was not significantly affected by the treatment with morphine. In contrast with male rats, the binding capacity of cytochrome P-450 for hexobarbital and aminopyrine was not affected by the treatment with

morphine in female rats. Similar pattern of the alterations in the binding capacity of cytochrome P-450 was observed in microsomes from fasted rats. In male rats, castration decreased the binding capacity for hexobarbital and aminopyrine and this was restored by treatment with methyltestosterone. The administration of morphine did not cause a further decrease in the binding capacity in castrated rats, while a clear decrease was caused in the methyltestosterone-treated castrated rats. The Km value for hexobarbital hydroxylation and the Ks (spectral dissociation constant) value for the hexobarbital-induced spectral change were both increased in microsomes from morphine-treated rats, whereas both values for aniline were not altered. These results suggest that the decrease in the binding capacity of cytochrome P-450 for hexobarbital and aminopyrine is due to the decrease in the oxidation of drugs by liver microsomes from morphine treated male rats. The impairment of the androgen-dependent regulatory mechanisms for the binding capacity of cytochrome P-450 seems to be a responsible factor for the decrease in the binding capacity of P-450 for hexobarbital and aminopyrine in morphine-treated male rats. 27 references. (author abstract modified)

63983
AUTHORS: York, D. H.
ADDRESS: Department of Physiology, Queen's University, Kingston, Ontario, Canada
TITLE: Possible dopaminergic pathway from substantia nigra to putamen.
SOURCE: Brain Research (Amsterdam).
SOURCEID: 20(2):233-249, 1970.

Evidence is presented suggesting that dopamine is a synaptic transmitter in the putamen, released from the terminals of axons whose cell bodies lie in the substantia nigra. Electrical stimulation of the substantia nigra (SN) with single rectangular pulses resulted in a negative focal potential being recorded in the putamen. An action potential was often associated with the negative focal potential. The latency of such SN-evoked units varied between 4.5 and 10 msec, indicating that the nigro -putamen fibers conduct impulses quite slowly (0.6 to 1.4 m/sec) and are of small diameter, probably consisting of C-type fibers. This is in agreement with fluorescent microscopy findings of poorly myelinated dopamine-containing fibers. An increase in the neuronal discharge frequency caused by both iontophoretically applied dopamine and repetitive stimulation of the substantia nigra was observed with 43 neurones (77%). This excitant action was blocked more readily by alpha-adrenergic antagonists and on a few occasions potentiated by monoamine oxidase inhibitors. On other neurones (37 in number) dopamine caused a depression of neuronal discharge which was antagonized more successfully by beta-adrenergic blocking drugs. Several other monoamines were tested on neurones in the putamen including L-noradrenaline, p-tyramine, L-DOPA, homovanillic acid and 5-hydroxytryptamine. The actions of L-DOPA and homovanillic acid, the precursor and breakdown product of dopamine, were weak in comparison to those of dopamine. 58 references. (author abstract)

63993
AUTHORS: Roux, C.; Dupuis, R.; Aubry, M.
ADDRESS: Laboratoire d'Embryologie, Faculte de Medecine, St. Antoine, Paris, France
TITLE: LSD: no teratogenic action in rats, mice, and hamsters.
SOURCE: Science.
SOURCEID: 169(3945):588-589, 1970.

To test the teratogenic properties of LSD, lysergic acid diethylamide tartrate was given to 98 pregnant rats, 67 mice, and 22 hamsters as a single dose of 5 to 500 micrograms per kilogram of body weight per day either at the beginning of gestation or during the period of organogenesis. Examination of the 1003 rat fetuses, 521 mouse fetuses, and 189 hamster fetuses obtained failed to prove any abortifacient, teratogenic, or growth-depressing effects. 11 references. (author abstract modified)

64000
AUTHORS: Marcucci, F.; Mussini, E.; Fanelli, R.; Garattini, S.
ADDRESS: Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, 20157 Milan, Italy
TITLE: Species differences in diazepam metabolism -- I. Metabolism of diazepam metabolites.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(5):1847-1851, 1970.

Male Sprague-Dawley rats and male albino Swiss mice were intravenously administered 5mg/kg N-demethyldiazepam, N-methyloxazepam or oxazepam to determine the distribution and metabolism of these metabolites. The changes in concentration with time were determined by gas chromatography. The peak following N-demethyldiazepam administration for blood and brain occurred immediately after injection; in adipose tissue there was a progressive increase up to 30 minutes after injection. The distribution pattern of N-methyloxazepam was similar. The peak following oxazepam injection occurred in blood and brain after 1 to 5 minutes, while the adipose tissue peak was reached at 30 minutes. The observed low rate of formation of N-demethyldiazepam when diazepam is incubated with rat liver microsomal enzymes is the limiting factor for the lack of accumulation of N-demethyldiazepam in rats. In mice oxazepam is retained for longer time than in rats, hence the administration of diazepam results in the presence of oxazepam only in mice and not in rats. 8 references.

64001
AUTHORS: Topham, J. C.
ADDRESS: Biochemistry Department, Imperial Chemical Industries, Ltd., Mereside, Alderley Park, Macclesfield, Cheshire, England
TITLE: Relationship between difference spectra and metabolism: barbiturates, drug interaction and species difference.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(5):1695-1701, 1970.

The characteristics of difference spectra induced by a series of barbiturates in a rat liver microsomal system are presented. No difference spectra were induced by barbital, N-methyl barbital and N,N'dimethyl barbital, but if the size of 1 of the substituents on C5(R5) was increased, Type I difference spectra were induced. Increasing chain length of aliphatic substituents at C5 resulted in a progressive decrease in dissociation constant. Substitution with phenyl or cyclohexenyl groups at C5 also included Type I difference spectra. Those oxybarbiturates which have a methyl group as the other substituent at C5(R4) have lower dissociation constants than the corresponding ethyl substituted compounds. The replacement of oxygen by sulfur in the barbital molecule as the substituent at C2(R2) resulted in the induction of a strong Type II difference spectrum, as did the compound thiophenobarbitone. Type I spectra were obtained from thiopentone and thialbarbitone. Characteristics of the difference spectra were also correlated with inhibition of the pharmacological action of tremorine, the potentiation of hexobarbital sleeping time by propranolol, and species differences in metabolism. 27 references.

64045
AUTHORS: Mandel, H. George; Triester, Sharon R.; Szapary, Daniele.
ADDRESS: Department of Pharmacology, George Washington University, School of Medicine, Washington, D.C.
TITLE: Interference of barbiturates with pyrimidine incorporation -- III: studies on the mechanism of the amobarbital-orotate relationship.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(6):1879-1892, 1970.

Previously observed inhibitory effect of various barbiturates on the uptake of orotate into Bacillus cereus was explored in greater detail. The effect was demonstrated for cells incubating at 0 degrees or in the presence of compounds interfering with energy conversion. Although it was not possible to measure intracellular orotate pools, it was concluded that amobarbital prevented the membrane associated transport of orotate, a process which apparently involved facilitated diffusion. The amobarbital effect was still observed under conditions of hypertonicity, did not include alterations in potassium flux, and appeared to be unrelated to biochemical effects of barbiturates described in mammalian species. Indeed, it was clearly demonstrable only in Bacillus cereus or in the closely related Bacillus subtilis. Two chemically unrelated compounds known to affect the functions of cellular membranes also prevented the incorporation of orotate into Bacillus cereus. Chlorpromazine and phenethyl alcohol inhibited 14C-orotate uptake into polynucleotides by about 50 percent, while the corresponding effect on 14C-uracil uptake was about 10 percent; phenethyl alcohol and amobarbital potentiated each other in their inhibition of orotate uptake. Thus, phenethyl alcohol probably behaves differently from amobarbital and structurally related derivatives, even though both appear to interfere with the bacterial membrane orotate transport system. Radioactivity was associated with cells of Bacillus cereus after incubation with 14C-pentobarbital, but no cellular concentration was observed. Orotate did not have a reciprocal effect on the disposition of the barbiturate. Washing with medium readily removed almost all pentobarbital from the cells. 35 references. (author abstract)

64046
AUTHORS: Mandel, H. George; Riis, Margit.
ADDRESS: Department of Pharmacology, George Washington University, School of Medicine, Washington, D.C.
TITLE: Interference of barbiturates with pyrimidine incorporation -- II: structural specificity of the inhibition of orotate uptake in bacillus cereus.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(6):1867-1877, 1970.

The structural specificity of the previously observed selective inhibition by amobarbital of the uptake of 2-14C- or 6-14C-orotate into exponentially growing cells of Bacillus cereus was examined. The effect of the drug was specific for the uptake of orotate and was not demonstrated for other labeled organic acids. None of several normal metabolites competed with orotate for transport into the cell. A series of other barbiturates, all at 1mM, inhibited the orotate uptake system without concomitantly affecting the incorporation of uracil into cellular pyrimidines. Phenobarbital, barbital, thiopental, pentobarbital and amobarbital were most active in the model system, as was the convulsant 5(1,3 dimethylbutyl)-5-ethylbarbituric acid. Barbituric acid itself was inactive and N-substitution, as in hexobarbital, reduced activity. Certain substitutions in the phenobarbital molecule led to loss of activity in the system, indicating structural requirements for interference with the uptake system. Attempts to relate the relative loss of activity to the extent of ionization and lipid solubility were only partially successful. The closely related hydantoin derivative, phenylethylhydantoin, was extremely active. Diphenylhydantoin also interfered with orotate uptake, whereas pheneturide, an open chain derivative, was completely inactive. It is concluded that these drugs, many of which have important sedative or anticonvulsant properties, inhibit the transport system for orotate in the bacteria. The structural components apparently required for activity in the system have been described. 16 references. (author abstract)

64050
AUTHORS: Vaccari, Andrea; Vertua, Rodolfo.
ADDRESS: University Institute of Pharmacology, Faculty of Pharmacy,

Via Capo S. Chiara 5, Genoa, Italy
TITLE: 14C-5-hydroxytryptamine and 3H-D-amphetamine: uptake and contraction by the rat stomach fundus in vitro.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(6):2105-2115, 1970.

The uptake of radioactive 5-hydroxytryptamine (5-HT) and D-amphetamine (DA) after enzymatic alteration of the receptors by neuraminidase and ethylenediaminetetracetate disodium salt (EDTA) and after receptor blockade by lysergic acid diethylamide (LSD) was studied. The binding of radioactively labeled 5-HT and DA by the isolated rat fundal smooth muscle was found independent of contraction. After a short incubation period the 2 amines bound to extrareceptor sites which were not related to smooth muscle contraction. The uptake of both amines by normal tissues was similar after treatment with neuraminidase plus EDTA (5-HT receptor destruction) and after preincubation with LSD. This may support the hypothesis of a common receptor system for both 5-HT and DA. Neuraminidase also had a relatively aspecific effect on the cell membrane. 18 references. (author abstract modified)

64052
AUTHORS: Khanna, J. M.; Kalant, H.
ADDRESS: Department of Pharmacology, University of Toronto, Toronto, Ontario, Canada
TITLE: Effect of inhibitors and inducers of drug metabolism on ethanol metabolism in vivo.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(6):2033-2041, 1970.

The effects of pretreatment with SKF 525-A, chlorcyclizine and phenobarbital upon sleeping time and metabolism of ethanol under similar conditions were studied. SKF 525-A (beta-diethylaminoethyl diphenylpropyl acetate), in a dose of 50mg/kg (i.p.), had no effect on ethanol sleeping time or on the rate of disappearance of ethanol from the whole body in mice, or on the slope of linear decrease of blood ethanol concentration in rats. It appeared to delay the absorption or distribution of ethanol, as shown by a crossover in the blood curves. Chronic pretreatment with chlorcyclizine hydrochloride (50mg/kg) or phenobarbital sodium (100mg/kg), in doses which significantly shortened the pentobarbital sleeping time, had no effect on ethanol sleeping time or ethanol metabolism in rats, although onset of sleep was delayed in rats pretreated with phenobarbital. It was concluded that the hepatic microsomal drug metabolizing systems are probably not involved in ethanol metabolism in vivo, or in cross-tolerance between ethanol and other drugs. 21 references. (author abstract modified)

64053
AUTHORS: Van Winkle, Elnora; Schweitzer, Jack W.; Friedhoff, Arnold J.
ADDRESS: Department of Psychiatry, New York University School of Medicine, New York, New York
TITLE: Beta-hydroxylation of N-acetyl-3,4-dimethoxyphenethylamine and the influence of iproniazid on the demethylation of this compound in vivo in the rat.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(6):2137-2144, 1970.

3,4-Dimethoxyphenethylamine (DMPEA) in human urine may be of possible significance in the biochemistry of mental disorders. N-acetyl-3,4-dimethoxyphenethylamine (NADMPEA), a metabolite of DMPEA, was studied to determine the effect of iproniazid on its degradation. Male rats were injected with iproniazid (80mg/kg) 5.5 and 1.5 hr prior to injections of DMPEA or NADMPEA. Urine was collected for 16 hr.
N-acetyl-beta-hydroxy-3,4-dimethoxyphenethylamine was found in the urine of rats after intraperitoneal administration of either 3,4-dimethoxyphenethylamine or N-acetyl-3,4 -dimethoxyphenethylamine.

Identification was made from chromatographic, cocrystallization and mass spectral data. The monoamine oxidase inhibitor, iproniazid, was found to diminish the extent of demethylation of N-acetyl-3,4-dimethoxyphenethylamine in vivo by 17 percent. 28 references. (author abstract modified)

64056
AUTHORS: Salama, A. I.; Goldberg, M. E.
ADDRESS: Department of Pharmacology, Warner Lambert Research Institute, Morris Plains, New Jersey 07950
TITLE: Neurochemical effects of imipramine and amphetamine in aggressive mouse-killing (muricidal) rats.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(6):2023-2032, 1970.

The kinetics of brain norepinephrine and serotonin in the mouse killing rat (muricidal) and the influence of imipramine and amphetamine on norepinephrine turnover in this mode of aggression were studied. Male rats selected for positive mouse killing response were sacrificed 24 hr after the last presentation of mice. Mouse killing rats were shown to have higher forebrain levels of norepinephrine than control nonkiller rats. In addition, they elicited higher rate constants for the decline of 3H-norepinephrine given intraventricularly into the brain and, consequently, much higher turnover rates for norepinephrine than controls (nonkillers). These differences were not obtained in the hindbrain region. No differences in the levels or rate of turnover of serotonin was observed in either brain region studied. Furthermore, the elevated rate constant seen in forebrain norepinephrine turnover studies using the isotopic procedure was not observed in nonisotopic turnover studies in which alpha-methyl-p -tyrosine was used to inhibit tyrosine hydroxylase. Differences between the two methods may be attributable to the inhibitory action of muricidal behavior by alpha-methyl-p-tyrosine. The effects of imipramine and amphetamine on norepinephrine turnover in the forebrain of killer rats were compared with those of drug-treated, nonkiller rats as well as with untreated rats. Both agents, given at doses which inhibit mouse-killing behavior, accelerate the turnover rate of brain norepinephrine in nonkiller rats; however, they did not influence the previously-elevated levels of norepinephrine nor the elevated rate constants and turnover rate for this amine in killer rats. Suggestions involving altered reuptake mechanisms, as well as divergent effects of the antidepressants in muricidal rats, were offered to explain these differences. 38 references. (author abstract modified)

64094
AUTHORS: Huang, C. L.; Yeh, J. Z.
ADDRESS: Department of Pharmacology, School of Pharmacy, University of Mississippi, University, Mississippi
TITLE: Distribution, excretion and metabolism of trifluoperazine methiodide-C14 in rats.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(3):235-242, 1970.

The rate of absorption and elimination of trifluoperazine methiodide-C14 was studied by demonstrating tissue distribution and urinary and fecal excretion of this compound in rats. Rats were injected with trifluoperazine methiodide-C14 (1mg, i.p.) and their feces and urine were collected every 8 hr. It was found that most of the trifluoperazine methiodide-C14 was excreted in feces by rats. No radioactivity was detected in the expired air of the animals. Blood level was generally low but detectable with a peak level at 1 hr; however, the brain level was insignificant against the background at all times. Antimicrobial activities have been demonstrated. Metabolic studies indicated that the majority of this compound was excreted unchanged. 17 references. (author abstract modified)

64096
AUTHORS: Stolk, J. M.; Bech, R. H.
ADDRESS: Department of Psychiatry, Stanford University, School of Medicine, Stanford, California 94305
TITLE: Antagonism of D-amphetamine by alpha-methyl-L-tyrosine: behavioral evidence for the participation of catecholamine stores and synthesis in the amphetamine stimulant response.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(3):249-263, 1970.

The ability of alpha methyl-L-tyrosine to antagonize the locomotor stimulant effects of D-amphetamine was tested in rats pretreated with saline, pheniprazine or reserpine. Dose alpha-methyl-L-tyrosine-antagonism curves in saline pretreated rats were shown to be dependent upon the challenging dose of amphetamine employed. After 1mg/kg of the stimulant, no antagonism of the evoked locomotor stimulation was observed at doses of the amino acid below 25mg/kg. Stimulation to 2 and 4mg/kg amphetamine, on the other hand, was significantly antagonized by much lower doses of alpha-methyltyrosine. Pheniprazine-pretreated rats were more sensitive to the effects of amphetamine, but less prone to antagonism by the amino acid. The locomotor stimulation to the sympathomimetic amine in the reserpine-pretreated rats was inhibited by very low doses of alpha-methyl-L-tyrosine. These data are interpreted to reveal a participation of both endogenous catecholamine stores and biosynthesis in the amphetamine response in saline-pretreated rats. Pheniprazine increases the relative importance of stores, whereas reserpine pretreatment leaves the animals completely dependent upon catecholamine biosynthesis for realization of amphetamine-induced locomotor stimulation. 36 references. (author abstract)

64100
AUTHORS: Felpel, L. P.; Sinclair, J. G.; Yim, G. K. W.
ADDRESS: Department of Physiology, Rockefeller University, New York, New York
TITLE: Effects of morphine on Renshaw cell activity.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(3):203-210, 1970.

The unit activity of Renshaw cells was monitored by means of extracellular microelectrodes to directly test the action of morphine on the motor - axon collateral Renshaw cell synapse. It was found that morphine (5-10mg/kg i.v.) reduced recurrent inhibition but had no effect on direct inhibition of a spinal monosynaptic reflex in decerebrate and pentobarbitone-anesthetized cats. Using extracellular glass microelectrodes to record unit activity from Renshaw cells, it was found that Renshaw cell discharges evoked by ventral root stimulation and by intravenous nicotine were not significantly depressed by morphine. Hence, the reduction of recurrent inhibition by morphine cannot be ascribed to an action at the synapse of the motor - axon collateral on Renshaw cells. 22 references. (author abstract modified)

64101
AUTHORS: Behroozi, K.; Assael, M.; Ivriani, I.; Nir, I.
ADDRESS: Hebrew University, Hadassah Medical School, Jerusalem, Israel
TITLE: Electrocortical reactions of pinealectomized and intact rats to lethal doses of pentobarbital.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(3):219-22, 1970.

Electrical activity of the brain was studied after administration of lethal doses of pentobarbitone in pinealectomized, sham operated and intact rats. Electrocorticograms (ECoG) and electroencephalograms (EEG) were recorded from silver electrode implants following sodium pentobarbitone (70mg/kg, i.p.) injection. Pinealectomized animals showed spiky wave discharges 3 minutes following injection from ECG electrodes, whereas no electrical

activity was apparent in control rats. At 5 min, pinealectomized animals showed monorhythmic, bilateral and regular activity (20 to 50 microvolts) compared with polyrhythmic, polymorphic activity in controls, and discharges became spiky at 7 min in the pinealectomized rats. After 9 mins, electrical activity disappeared in control animals while pinealectomized rats showed continued activity which ceased at the 15th minute. The enhanced excitatory level of the central nervous system due to pinealectomy appears to delay the effect of lethal doses of barbiturate. 2 references.

64144
AUTHORS: Rosenblatt, S.; Leighton, W. P.; Chanley, J. D.
ADDRESS: Department of Psychiatry, The Mount Sinai School of Medicine, New York, New York 10029
TITLE: A novel approach to the investigation of norepinephrine metabolism in human sympathetic nerve.
SOURCE: Journal of Neurochemistry (London).
SOURCEID: 17(7):1105-1108, 1970.

Metabolites of injected (7-3H) norepinephrine (1mCi, i.v.) found in human saliva were studied during a resting phase and following gustatory stimulation (1ml of 0.5 molar citric acid swirled in mouth and swallowed) by liquid scintillation spectrometry. Although both rate of secretion of saliva (ml/min) and radioactive metabolites (c.p.m./min) increased (resting: .6 ml/min, 300 c.p.m./min; stimulation: 2.8 ml/min, 1408 c.p.m./min) upon stimulation, the percentage increase in salivary flow was usually greater than that of the metabolites, as indicated by the decrease in concentration of radioactive material in saliva (c.p.m./ml) following stimulation. Gustatory stimulation apparently had a slightly greater effect on parasympathetically-induced salivary flow than on sympathetically induced activity. Following gustatory stimulation, there was also a change in the distribution of radioactive metabolites. In resting and stimulated saliva, 3 peaks of radioactivity, accounting for 97 to 99% of the applied radioactivity were observed in 2 chromatographic systems. The distribution of metabolites (3-methoxy-4-hydroxyphenylglycol, vanillomandelic acid, normetanephrine) during rest was 54, 40 and 5% respectively and following stimulation, 33, 60 and 4%, respectively. The approach presented may provide a method of investigating in vivo the metabolism of norepinephrine in a single organ in man under a variety of physiological and pharmacological conditions. 10 references.

64146
AUTHORS: Azmitia, Efrain C.; Hess, Paul; Reis, Donald.
ADDRESS: The Rockefeller University, New York, New York 10021
TITLE: Tryptophan hydroxylase changes in midbrain of the rat after chronic morphine administration.
SOURCE: Life Sciences (Oxford).
SOURCEID: 9(11):633-637, 1970.

The increase in serotonin turnover induced by morphine may be due to a de novo synthesis of tryptophan hydroxylase, the rate-limiting enzyme in serotonin metabolism. The changes in tryptophan hydroxylase activity during a tolerance withdrawal cycle to morphine in the midbrain of rats (female, Sprague-Dawley) was investigated. Forty rats were divided into 4 groups: an unhandled control group, a tolerant group, a withdrawal group and a saline control group. The tolerant and withdrawal groups received morphine sulfate (5mg/kg twice a day increasing to 95mg/kg three times a day, s.c.) over a 16-day period. At the end of this period, the tolerant group was sacrificed 2 hr after a final injection of 130mg/kg. The withdrawal group was sacrificed 48 hr after an injection of the same dose. The saline control group received injections of equal volume of isotonic saline on the same schedule as the tolerant group. The saline group demonstrated a significant increase in tryptophan hydroxylase activity as compared with the unhandled controls. The enzyme level in tolerant animals showed a 40% and a 17% increase when compared with unhandled controls and saline group respectively. Hence, tolerance

to morphine is accompanied by an enzyme increase in the midbrain which is consistent with the reported increase of serotonin turnover. After a 48-hr withdrawal period, the enzyme level had dropped from its tolerant level but still remained elevated when compared with unhandled controls. The effects of morphine in increasing brain tryptophan hydroxylase activity may be partially mediated by hormonal induction, since it is well known that morphine is a powerful activator of the pituitary adrenal axis. 10 references.

64161
AUTHORS: Wurtman, R. J.; Chou, C.; Rose, C.
ADDRESS: Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139
TITLE: The fate of C14-dihydroxyphenylalanine (C14-dopa) in the whole mouse.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 174(3):351-356, 1970.

The metabolic fate of i.p. administered C14-DL-dopa was examined in the whole mouse. The amino acid was rapidly destroyed at an initial rate (7.3% of injected dose per min) that was maintained for almost 10 minutes. This level of C14-catecholamine in the whole carcass reached a peak 20 minutes after injection; almost all of this material was C14-dopamine. Less than 0.1% of the C14-catechols present in the body 20 or 60 minutes after C14-DL-dopa administration was found the brain. At all doses studied (0.5-150mg/kg), more than half of the C14-dopa was metabolized during the first 20 minutes after its administration to C14-methoxydopa and C14-homovanillic acid. If the metabolism of the circulating amino acid in humans is similar to that of mice, it can be calculated that the amount of methionine needed to O-methylate the doses of L-dopa commonly used in parkinsonian patients may be greater than the average daily methionine intake. 24 references. (author abstract)

64167
AUTHORS: Slotkin, Theodore A.; DiStefano, Victor.
ADDRESS: Department of Pharmacology, University of Rochester, Rochester, New York
TITLE: A model of harmine metabolism in the rat.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 174(3):456-462, 1970.

Previous work from this laboratory has shown that the urinary metabolites of harmine (I) in the rat are harmol (II), harmol glucuronide (III) and harmol sulfate (IV); the rate limiting step in harmine metabolism is first order with respect to the amount of harmine remaining in the body and occurs before the conjugation reactions. In the present study, biliary and urinary levels of the metabolites were determined after an i.v. dose of 5mg/kg of I to rats; tissue levels of I were determined over a four-hour period. Metabolites were separated by paper chromatography; conjugates were hydrolyzed with beta-glucuronidase-aryl sulfatase and the concentrations of I and II were determined by quantitative fluorometry. More than 99 percent of the dose was recovered; 73 percent was in the bile and 26 percent was in the urine. Nearly 70 percent was excreted in the first four hours. Seventy-seven percent was excreted as IV, 21 percent as III and 1 percent as I and II. Excretion of IV leveled off after 8 hours, whereas excretion of III accelerated, probably due to sulfate depletion. The excretion curve indicated that two compartments contributed to the rate-limiting step. The levels in I in muscle corresponded to one of these compartments, and the levels in the other tissues corresponded to the second compartment. With the experimental data, a model of harmine metabolism was constructed which gave theoretical excretion curves which agreed with the experimental values to within 5 percent. 8 references. (author abstract)

64170
AUTHORS: Lemberger, Louis; Witt, Ellen D.; Davis, John M.; Kopin, Irwin J.
ADDRESS: Laboratory of Clinical Science, National Institute of Mental Health, Bldg. 10, Room 2D-46, Bethesda, Maryland 20014
TITLE: The effects of haloperidol and chlorpromazine on amphetamine metabolism and amphetamine stereotype behavior in the rat.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 174(3):428-433, 1970.

Chlorpromazine has been used for the treatment of severe amphetamine toxicity. The present investigation compares the effects of chlorpromazine and haloperidol on amphetamine metabolism and the ability of each to block amphetamine stereotype behavior. In rats treated with chlorpromazine (15mg/kg) or haloperidol (10mg/kg) 30 minutes prior to the administration of tritiated amphetamine, there was a slowing of the disappearance of tritiated amphetamine from the brain. The half-life of the labeled amine increased to 140 minutes after chlorpromazine and to 69 minutes after haloperidol from a control value of 52 minutes in saline pretreated control rats. After pretreatment with chlorpromazine (15mg/kg) or haloperidol (10mg/kg) only 29% and 80% (respectively) of the administered tritiated-amphetamine was metabolized in 3 hours by the whole rat as compared to 93% of the administered dose in control animals. Haloperidol (0.5mg/kg) completely blocked amphetamine stereotype behavior whereas chlorpromazine in doses of 1 and 5mg/kg only partially blocked this effect. Haloperidol in a dose which blocked amphetamine stereotype behavior had no inhibitory effect on amphetamine metabolism. 17 references. (author abstract)

64177
AUTHORS: Stone, W. E.
ADDRESS: Department of Physiology, University of Wisconsin, Madison, Wisconsin 53706
TITLE: Convulsant actions of tetrazole derivatives.
SOURCE: Pharmacology (Basel).
SOURCEID: 3(6):367-370, 1970.

Tetrazole derivatives, including several newly synthesized compounds, were tested on mice. In the unsubstituted cyclopolymethylenetetrazole series, the hepta-compound exhibited maximum convulsant potency. The activity of the penta-compound is greatly increased by 8-substitution of a tertiary butyl group. It is increased by 6-monosubstitution of chlorine, and increased to a greater extent by 6,6prime-disubstitution of chlorine. The potency of the hexa-compound also is increased by 6,6prime-disubstitution of chlorine. Introduction of bromine is less effective; 6,6prime-disubstitution in the tetra-compounds and penta-compounds gave products of low solubility that were inactive at dose levels attained. Several 5-monosubstituted tetrazoles showed no convulsant effects; of these, 5-methyltetrazole and 5-propyltetrazole showed high toxicity. 7 references. (author abstract)

64180
AUTHORS: Lee, N. H.; Min, K. S.; Hong, S. S.
ADDRESS: Department of Pharmacology, Yonsei University, College of Medicine, Seoul, Korea
TITLE: The effects of phenobarbital on exocrine pancreas.
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (Gand).
SOURCEID: 185(2):350-356, 1970.

The effect of phenobarbital as an enzyme inducer in the pancreatic microsomal system was studied. It was found that daily administration of phenobarbital (75mg/kg) in rats significantly increased the activities of amylase and lipase both in pancreatic tissue and juice. However, trypsin was unaffected either in the juice or in the pancreatic tissue. These data indicate that

pancreatic enzymes can be stimulated by treatment with phenobarbital. The biliary secretion in the phenobarbital-treated group was markedly elevated as compared with untreated control. Although the concentration of bilirubin in the bile was not significantly different, the total bilirubin output was 40 to 50 percent higher in phenobarbital-treated animals than that in controls. The concentration of cholate in the bile was significantly lower in the treated group than that in the control group. This suggests that phenobarbital treatment may alter cholesterol metabolism. 22 references. (author abstract modified)

64254
AUTHORS: Glover, A. B.; McCulloch, M. W.
ADDRESS: Department of Pharmacology, University of Melbourne, Parkville, Victoria 3052, Australia
TITLE: Interaction between reserpine and desmethylimipramine.
SOURCE: European Journal of Pharmacology (Amsterdam).
SOURCEID: 11(2):163-168, 1970.

The effects of desmethylimipramine (1mg/kg) and reserpine (2.5 mg/kg) were studied on pressor responses to sympathetic stimulation in pithed rats. Drugs were administered through a cannula in the femoral or jugular vein in pithed rats and intraperitoneally in intact rats. Reserpine was more effective in decreasing the pressor response to sympathetic stimulation if it was administered to rats with the central nervous system intact. There was no interaction between reserpine and desmethylimipramine (1mg/kg) if the drugs were administered after pithing, but if they were administered before pithing, desmethylimipramine delayed the onset of action of reserpine. It is concluded that the action of reserpine in depleting noradrenaline from peripheral sympathetic neurons involves the central nervous system and the interaction between reserpine and desmethylimipramine is confined to central adrenergic mechanisms. 26 references. (author abstract modified)

64255
AUTHORS: Bartosek, I.; Mussini, E.; Saronio, C.; Garattini, S.
ADDRESS: Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, 20157 Milan, Italy
TITLE: Studies on nitrazepam reduction in vitro.
SOURCE: European Journal of Pharmacology (Amsterdam).
SOURCEID: 11(2):249-253, 1970.

Several experiments were conducted to establish the degree of nitrazepam reduction in vitro by various organs (liver, kidney, heart, lung, skeletal muscle, spleen preparation, brain) by various animal species (rats, mice, rabbits, guinea pigs) and the influence of various inhibitors and experimental conditions on this enzymatic process. Solvents decreased the reduction rate of nitrazepam by rat liver homogenate; the lowest interference was observed with ethanol. High concentrations of nicotinamide used in media for nitroreductase determination lowered enzyme activity. Reduction of nitrazepam to the 7-amino derivative decreased during the preservation of liver centrifugal fractions in 1.15% KCl at 0 degrees C. The highest enzyme activity was found in rat liver, followed by the activity of kidney, heart, lung, skeletal muscle and spleen preparations. The substance was not reduced in brain. The Michaelis constants of nitrazepam reduction did not differ substantially, being of the same order in preparations from rat, mouse, rabbit and guinea pig liver. The maximal velocities of the reduction were .000001 moles per hour per 1 g of liver tissue. Chlorpromazine, diazepam and imipramine influenced the reduction only in high concentrations. Ethylenediaminetetraacetic acid, cysteine and ascorbic acid did not substantially change the enzyme activity. Potassium cyanide was a strong noncompetitive inhibitor of the nitrazepam reduction. 8 references. (author abstract modified)

64261
AUTHORS: Huang, C. L.; Mir, G. M.; Yeh, J. Z.
ADDRESS: School of Pharmacy, University of Mississippi, University, Mississippi 38677
TITLE: Distribution, excretion, and metabolism of 14C-labeled quaternary ammonium salt of perphenazine in rats.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(7):976-979, 1970.

The distribution, excretion and metabolism of the 14C-labeled quaternary ammonium salt of perphenazine were studied in Holtzman rats. Intraperitoneally-administered perphenazine dimethiodide-14C (1mg) was well absorbed by the rats. Forty percent of the drug was accumulated in the kidneys and was excreted in the urine; only 14% of the drug was excreted by the intestines. The ratio of the urinary to fecal excretion was 2.8 to 1. Peak blood level was observed 0.5 hr after the administration of the drug. Perphenazine dimethiodide-14C seemed to have a particular affinity for the bone. The activity in the bone started to rise in 0.5 hr and reached its peak level in 1 hr. Brain level was low but above the detectable level at 0.5 hr. Excretion of the activity of perphenazine dimethiodide-14C was fairly rapid; almost 70% of the activity, excreted in urine and feces, was recovered in the first 32-hr period. The quaternary ammonium salt of this compound has a toxicity higher than the parent compound, perphenazine. Antibacterial activities against gram-positive and gram-negative bacteria was demonstrated. 11 references. (author abstract modified)

64263
AUTHORS: Singh, Jasbir M.; Fiegenschue, Bruce; Schexnaydre, Carl.
ADDRESS: Department of Pharmacology, College of Pharmacy, Xavier University, New Orleans, Louisiana 70125
TITLE: Development of tolerance to pentobarbital.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(7):1020-1022, 1970.

The development of tolerance to pentobarbital was studied using female albino rats. Pentobarbital was administered intraperitoneally in a dose of 25mg/kg to 5 different groups of rats at various time intervals. Tolerance to pentobarbital developed 4 hr after the first injection and reached a peak at 17 to 22 hr, after which it decreased to nonsignificant levels by 48 hr. The duration and frequency of administration of pentobarbital affected the degree of development of tolerance to pentobarbital. Percentage Tolerance Index (PTI) decreased progressively with the increase in the number of injections. When 4 injections were given within the span of 28 hr, the animals showed a greater degree of tolerance on the third injection which was administered 24 hr after the initial injection. Tolerance was also present on the fourth injection but to a lesser degree when compared with the third injection. The experimental data from this study suggest that tolerance to pentobarbital does develop and is the result of the pentobarbital stimulating its own metabolizing enzyme. 11 references. (author abstract modified)

64282
AUTHORS: Salvador, R. A.; Atkins, C.; Haber, S.; Conney, A. H.
ADDRESS: Wellcome Research Laboratories, Burroughs Wellcome & Company, Tuckahoe, New York 10707
TITLE: Changes in the serum concentration of cholesterol, triglycerides and phospholipids in the mouse and rat after administration of either chlorcyclizine or phenobarbital.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(4):1463-1469, 1970.

The changes in serum concentration of cholesterol, triglycerides, and phospholipids, in liver concentration of cholesterol and triglyceride, and in body and liver weight were studied following the administration (ad lib) of phenobarbital, chlorcyclizine, and analogs of chlorcyclizine in mice and rats. Chlorcyclizine (0.08%, 0.04%, and 0.01%) and phenobarbital (0.05%)

lowered the serum levels of cholesterol, triglyceride and phospholipids but did not affect the liver concentrations of cholesterol or triglyceride in male mice, while chlorcyclizine at the higher doses reduced body weight and increased the liver weight. The serum levels of cholesterol and phospholipid were not always reduced by chlorcyclizine in the rat, but serum triglyceride was markedly reduced by all doses, and liver triglyceride and cholesterol tended to increase. Norchlorcyclizine and N-ethyl-N (prime) benzhydrylpiperazine significantly reduced serum levels of cholesterol and triglyceride in mice, but apparently analogs without the benzhydryl portion of the molecule do not. 10 references.

64288
AUTHORS: Sharkawi, M.
ADDRESS: Department of Pharmacology, Faculty of Medicine, University of Montreal, Montreal, Quebec, Canada
TITLE: Effects of morphine and pentobarbitone on acetylcholine synthesis by rat cerebral cortex.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 40(1):86-91, 1970.

The synthesis of carbon-14-labeled acetylcholine (14C-ACh) from carbon-14 uniformly labeled glucose (U-14C-D-glucose) under different conditions was studied. The ability of cerebral cortex slices and minces from morphine-treated and pentobarbitone-treated rats incubated in 4 mM K ion medium to form 14C-ACh was markedly reduced as compared with those from control animals. The ability of slices from drug-treated and control animals incubated in 31 mM K ion medium to form 14C-ACh was similar. Cerebral cortex homogenates from both groups of animals in either 4 or 31 mM K ion medium formed similar amounts of 14C-ACh. These findings add further support to the hypothesis that the concentration of acetylcholine at the site of synthesis governs the rate of formation of the neurotransmitter. 17 references. (author abstract)

64290
AUTHORS: Ireson, J. D.
ADDRESS: Chemistry and Biology Department, Barking Regional College of Technology, Longbridge Road, Dagenham, Essex, England
TITLE: A comparison of the antinociceptive actions of cholinomimetic and morphine-like drugs.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 40(1):92-101, 1970.

The antinociceptive activity of morphine, nalorphine, oxotremorine and eserine has been examined in mice in electroshock and phenylbenzoquinone writhing tests. The effectiveness of these drugs alone, in combination with each other, and in combination with the muscarinic antagonist atropine sulphate, and with the narcotic antagonist naloxone has also been investigated. In both tests morphine was effective and antagonized by naloxone. Nalorphine was active in the phenylbenzoquinone test but only slightly active in the electroshock test: it was antagonized by naloxone in both tests. Morphine was potentiated by nalorphine in the phenylbenzoquinone test, but antagonized by it in the electroshock test. Oxotremorine was effective in both tests, and was antagonized by atropine sulphate. Eserine was active only in the phenylbenzoquinone test, and was antagonized by atropine sulphate. Oxotremorine was potentiated by eserine in the phenylbenzoquinone test, but antagonized by it in the electroshock test. Crossed agonist and partial agonist experiments produced enhancement. No antagonism was seen in the crossed antagonist experiments. The similarities between the effects of the two classes of drugs are discussed, and the conclusion drawn that they act by separate mechanisms. 11 references. (author abstract)

64364
AUTHORS: Ladisich, W.; Volbehr, H.; Matussek, N.

ADDRESS: Max-Planck-Institut fur Psychiatrie, Biochemische Abteilung, Kraepelinstrasse 2, 8 Munich 23, West Germany
TITLE: Paradoxical amphetamine effect in hyperactive rats in relation to norepinephrine metabolism.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(4):303-310, 1970.

Amphetamine had a paradoxical sedative effect in hyperactive rats pretreated with desmethylimipramine (DMI) and the benzoquinolizine Ro4-1284. Intracisternal injection of H3-NE was used to investigate the influence of the different drugs on norepinephrine (NE) metabolism. There was found to be a marked increase in normetanephrine (NM) after DMI-Ro4-1284 and amphetamine, compared with treatment by DMI-Ro4-1284 alone. An increase in NM levels resulted from different doses of iproniazid in place of amphetamine, sedation occurring with the higher NM levels. Sedation also occurred with cocaine. Pyrogallol did not decrease the NM values or the paradoxical amphetamine effect. Inhibiting serotonin synthesis with p-chlorophenylalanine did not influence the paradoxical amphetamine response either. It was concluded that high NM levels in combination with low NE values were responsible for these paradoxial reactions. It is likely that cocaine acted by inhibiting NE reuptake, iproniazid by blocking MAO, and amphetamine by a combination of both these mechanisms. 30 references. (author abstract)

64369
AUTHORS: Kawai, N.
ADDRESS: Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, New York 10032
TITLE: Release of 5-hydroxytryptamine from slices of superior colliculus by optic tract stimulation.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(4):395-397, 1970.

The release of 5-hydroxytryptamine (5-HT) from the superior colliculus in response to optic tract stimulation was confirmed and the effect of LSD on the release of 5-HT was studied. Slices of guinea pig superior colliculus were incubated in an artificial medium with labeled 5-hydroxytryptamine (3H-5-HT). After incubation, electrical stimulation was applied to the optic tract and efflux of 3H-5-HT was measured in the superfused medium. During the stimulation period a marked increase of 3H-5-HT was observed. This increase of 3H-5-HT was not found when LSD was applied in the incubation medium or when the optic tract was cut. 10 references. (author abstract modified)

64408
AUTHORS: Konig-Bersin, P.; Waser, P. G.; Langemann, H.; Lichtensteiger, W.
ADDRESS: Tulpenstrasse 10, CH-8051 Zurich, Switzerland
TITLE: Monoamines in the brain under the influence of muscimol and ibotenic acid, two psychoactive principles of amanita muscaria.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):1-10, 1970.

The concentrations of noradrenaline, dopamine and serotonin were measured in the brain of male albino mice and rats after intraperitoneal injections of muscimol (3mg/kg), ibotenic acid (16mg/kg) or LSD (10mg/kg). All 3 drugs induced a generalized increase of serotonin. When muscimol was administered to rats after pretreatment with p-chlorophenylalanine, a serotonin synthesis inhibitor, the serotonin concentration was still increased in midbrain and hypothalamus. Muscimol also caused a reduced accumulation of 5-hydroxyindoleacetic acid in rats pretreated with probenecid. There were differences in the action of the 3 compounds on the catecholamine concentration. Muscimol and LSD caused a decrease of the catecholamines. Ibotenic acid increased the

catecholamine concentration. Certain topographical differences were noted. The increase in the serotonin concentration in the hypothalamus and midbrain after muscimol may be due to a reduced turnover of serotonin. An increase in serotonin concentration and a decrease of 5-hydroxyindoleacetic acid in the rat brain are effects observed also with other psychotomimetic drugs such as LSD or psilocybin. 23 references. (author abstract modified)

64409
AUTHORS: Crammer, J. L.; Rolfe, Brenda.
ADDRESS: St. John's Hospital, Stone, Aylesbury, Buckinghamshire, England
TITLE: Metabolism of 14C-imipramine: III. Conversions by rat tissue.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):26-37, 1970.

When the brains of Wistar rats were extracted 1.25 hours after single intraperitoneal injections of radioactive imipramine some desmethylimipramine (DMI) was always found, together with comparable amounts of iminodibenzyl (IdB) and 2-hydroxyimipramine. The total radioactivity recovered from brain, (usually less than 0.2 percent of dose) did not rise on repeated daily injection but then proportions of DMI and IdB tended to be higher. Brain slices incubated for 2 hours at 37 degree C with radioactive imipramine produced DMI, IdB, and some didesmethylimipramine, but no hydroxylated metabolites. Liver slices produced more DMI, less IdB, a fair amount of 10-hydroxy DMI and comparable 2-hydroxyimipramine. Heart, kidney, lung and gut slices were also active in varying degrees. These findings are consistent with at least 2 different metabolic hypotheses of the way imipramine exerts its antidepressant action in man. 22 references. (author abstract)

64411
AUTHORS: Stromberg, Ulf.
ADDRESS: Department of Pharmacology, Fack, S-40033 Goteborg 33, Sweden
TITLE: DOPA effects on motility in mice; potentiation by MK 485 and dexchlorpheniramine.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):58-67, 1970.

Mice were given L-DOPA i.p. in doses ranging from 7.8 to 500mg/kg with and without previous administration of MK-485, a compound capable of inhibiting extracerebral dopa decarboxylase. In addition, dexchlorpheniramine together with MK-485 was given before L-DOPA to some of the animals. Spontaneous locomotor activity of the animals was measured and some preliminary biochemical determinations were performed of dopamine, noradrenaline and 5-hydroxytryptamine levels in brain. It was found, that L-DOPA had both depressant and excitatory effects on locomotor activity depending on dose, and that MK-485 caused a potentiation of both these effects, together with an increased dopamine production in the brain. Dexchlorpheniramine caused a further potentiation of the effects on activity, evidently without affecting the total dopamine level in the brain. On the basis of these data, it was concluded that even the depressant effects on motility, seen after administration of L-DOPA, are probably mediated at least in part centrally. Apparently MK-485 potentiates L-DOPA effects on activity, simply by letting more of the DOPA injected pass through the blood brain barrier and form dopamine intracerebrally. Further investigations are required to obtain information on the mechanism of the DOPA potentiating action of dexchlorpheniramine. 26 references. (author abstract)

64413
AUTHORS: Dhawan, K. N.; Jaju, B. P.; Gupta, G. P.
ADDRESS: K. G. Medical College, Lucknow-3, India

TITLE: Validity of antagonism of different effects of reserpine as test for anti-depressant activity.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):94-98, 1970.

The adynamic, ptotic, hypothermic and conditioned avoidance response blocking effects of reserpine were studied in normal rats and in rats subjected to electroconvulsions for 5 days. Prior exposure to electroconvulsions blocked only the hypothermic response of reserpine. The relevance of this observation to the screening of antidepressant drugs by studying the reserpine antagonism is discussed. The mechanism by which exposure to electroconvulsions prevents some of the effects of reserpine are not revealed by this work. 10 references. (author abstract modified)

64419
AUTHORS: Steinberg, H. I.; Smith, C. B.
ADDRESS: Department of Pharmacology, University of Michigan Medical School, Ann Arbor, Michigan 48104
TITLE: Effects of desmethylimipramine and cocaine on the uptake, retention and metabolism of H3-tyramine in rat brain slices.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):176-192, 1970.

The effects of desmethylimipramine (DMI) and cocaine on the uptake, metabolism and retention of H3-tyramine were determined by incubating H3-tyramine with slices from the hypothalamus, brainstem, parietal cortex and caudate of rat brain in Krebs-Ringer solution at 37C for 20 minutes. Slices from all areas synthesized H3-p-hydroxyphenylacetic acid (H3-p-HPAA) and H3-octopamine. Cocaine, when added to the incubation flask 15 min before the addition of H3-tyramine, caused a decrease in both H3-octopamine and H3-p-HPAA synthesis as well as a decrease in the amount of H3-tyramine retained. DMI, when added to the incubation flask 15 min before the H3-tyramine, caused a marked decrease in the synthesis of H3-octopamine but did not decrease the synthesis of H3-p-HPAA or diminish the retention of H3-tyramine. Similar results were obtained with slices from rats pretreated with DMI 1 hour before sacrifice. The inhibition of H3-octopamine synthesis caused by DMI, both in vivo and in vitro, was noncompetitive, whereas that produced by cocaine was competitive. Cocaine and DMI, when added to homogenates of hypothalamus, had no effect on the synthesis of either H3-p-hydroxymandelic acid or H3-p-HPAA. Thus, cocaine blocks the uptake of H3-tyramine at the neuronal membrane. In contrast, low doses of DMI do not prevent the uptake of H3-tyramine at the neuronal membrane and subsequent synthesis of H3-p-HPAA, but do prevent the uptake of H3-tyramine into the intraneuronal sites where it is converted into H3-octopamine. 20 references. (author abstract modified)

64421
AUTHORS: Eade, N. R.; Benton, K. W.
ADDRESS: Department of Pharmacology and Therapeutics, McGill University, Montreal 109, Quebec, Canada
TITLE: The effect of phenelzine and tranylcypromine on the degradation of meperidine.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):31-36, 1970.

The administration of meperidine to patients treated with monoamine oxidase inhibitors can produce lethal reactions of unknown etiology possibly due to interference with the degradation of meperidine. Mice were given phenelzine (40 micrograms/g) and tranylcypromine (5 micrograms/g) and kept in individual cages to avoid aggregation effects. At 1, 4 and 24 hours after administration of monoamine oxidase inhibitors, they were given meperidine (20 micrograms/g), killed at various time intervals and the total body content of meperidine determined. Phenelzine inhibited the

degradation of meperidine and in contrast to the prolonged effect of phenelzine on monoamine oxidase, this effect disappeared within 24 hours. Tranylcypromine had a similar but more prolonged effect. Chronic pretreatment with tranylcypromine did not increase the degree or duration of inhibition. Phenelzine reduced the LD50 of meperidine, an effect which also disappeared within 24 hours, whereas tranylcypromine had no effect on the LD50. Inhibition of meperidine degradation by monoamine oxidase inhibitors may contribute to the toxic reactions seen in man, but may not be the only mechanism involved. 22 references. (author abstract)

64423
AUTHORS: Holmes, D. E.; Piette, L. H.
ADDRESS: Department of Biochemistry, University of Hawaii, 1997 East West Road, Honolulu, Hawaii 96822
TITLE: Effects of phenothiazine derivatives on biological membranes: drug -induced changes in electron spin resonance spectra from spin-labeled erythrocyte ghost membranes.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):78-84, 1970.

A unique electron spin resonance, nitroxide spin label probe technique was used to detect interaction between phenothiazine derivatives and bovine erythrocyte ghost membranes. Effects of solubilizing agents before and after reacting the spin label with the ghosts indicated that at least 3 membrane sulfhydryl sites could be spin labeled. Drug-induced changes in electron spin resonance spectra from the spin-labeled membranes suggested that the drugs altered the protein structure of one of the spin-labeled sites. Membrane structural changes occurred in relation to the molecular structure and concentration of the phenothiazines. 16 references. (author abstract modified)

64427
AUTHORS: Leitz, F. H.
ADDRESS: Department of Physiology and Biochemistry, Schering Corporation, 86 Orange Street, Bloomfield, New Jersey 07003
TITLE: Mechanisms by which amphetamine and desipramine inhibit the metaraminol-induced release of norepinephrine from sympathetic nerve endings in rat heart.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):152-157, 1970.

The mechanisms by which amphetamine and desipramine inhibit themetaraminol-induced release of norepinephrine (NE) from sympathetic nerve endings in rat heart was studied. The net influx of metaraminol into sympathetic nerve endings of rat ventricle slices as well as the resultant efflux of NE was a function of the metaraminol concentration in the incubation fluid and reached a maximum at a concentration of about 400 nanograms/ml. Amphetamine in low concentrations (0.4 micrograms/ml) reduced the efflux of NE and the uptake of metaraminol to the same extent, indicating that amphetamine interfered with the metaraminol-induced release of NE only by reducing the uptake of the drug. In contrast, desipramine reduced the efflux of NE to a much greater extent than it blocked the uptake of metaraminol. These results indicate that desipramine interfered with the metaraminol-induced release of NE in 2 ways: 1) by reducing the uptake of metaraminol, and 2) by interfering with the action of metaraminol within the neuron, possibly by an action on the granules. 11 references. (author abstract modified)

64480
AUTHORS: Baumel, Irwin; DeFeo, John J.; Harbans, Lal.
ADDRESS: Department of Pharmacology and Toxicology, University of Rhode Island, Kingston, Rhode Island 02881
TITLE: Effect of acute hypoxia on brain-sensitivity and

metabolism of barbiturates in mice.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(2):193-197, 1970.

Acute exposure of mice to hypobaric hypoxia, or reduced oxygen at normal pressure, markedly potentiated barbiturate-induced hypnosis. The mice showed lower body concentration of pentobarbital on awakening and reduced rate of pentobarbital disappearance from the body during exposure to the hypoxic environment. These data suggest that acute exposure to hypoxia depresses in vivo metabolism of pentobarbital and enhances central nervous system sensitivity to the barbiturates. 17 references. (author abstract)

64621
AUTHORS: Larson, Merlin D.; Major, Mitchell A.
ADDRESS: Department of Anesthesiology, Stanford University Hospital, Stanford, California 94305
TITLE: The effect of hexobarbital on the duration of the recurrent IPSP in cat motoneurons.
SOURCE: Brain Research (Amsterdam).
SOURCEID: 21(2):309-311, 1970.

The effect of hexobarbital on duration of recurrent inhibitory postsynaptic potential (IPSP) was studied in 10 adult cats subjected to precollicular decerebration (A4,D5,L2) by electrolysis under ether anesthesia. Anesthesia was discontinued immediately after decerebration. The results showed that hexobarbital prolonged the recurrent IPSP in motoneurons. The effect was not attributable to a prolonged Renshaw cell discharge, since it was previously shown that equivalent doses shortened the Renshaw cell discharge. Removal of disinhibition did not seem likely because recurrent IPSPs were also prolonged by hexobarbital when there was no spontaneous firing of Renshaw cells. Since barbiturates prolong presynaptic inhibition, possibly by delaying diffusion of inhibitory transmitter away from receptor sites, this would also explain the results of this study. However, prolonged release of inhibitory transmitter or alteration of nonsynaptic membrane properties should also be considered. 13 references.

63616
AUTHORS: Grota, Lee J.
ADDRESS: University of Rochester School of Medicine and Dentistry, Rochester, New York
TITLE: Effects of dexamethasone on the development of emotionality and adrenocortical reactivity.
SOURCE: Proceedings of the American Psychological Association.
SOURCEID: 78:203-204, 1970.

The effects of selectively inhibiting the pituitary-adrenocortical system during fetal and early postnatal development of rats on emotionality and adrenocortical function at adulthood was investigated through the treatment with dexamethasone of pregnant females and young animals during 2 to 17 days of lactation. The reaction to handling test was used. The data obtained suggest that the development of emotionality and adrenocortical function does not depend on an intact adrenocortical system in the mother; that an adrenocortical system which is able to respond to environmental stimuli during infancy is one determinant of adrenocortical function at adulthood; and that the functional significance for the adult of a dexamethoasone altered adrenocortical system during infancy depends on the intensity of the stimulus used to activate the adrenocortical system. 3 references. (Author abstract modified)

63688
AUTHORS: Fibiger, Hans C.; Lytle, Loy D.; Campbell, Byron A.
ADDRESS: Department of Psychology, Princeton University, Princeton, New Jersey 08540
TITLE: Cholinergic modulation of adrenergic arousal in the developing rat.
SOURCE: Journal of Comparative and Physiological Psychology.
SOURCEID: 72(3):384-389, 1970.

The development of the antagonistic nature of the adrenergic and cholinergic systems in the rat was investigated. The cholinomimetic drug, pilocarpine, was found to decrease amphetamine-induced psychomotor excitation in 20 to 25 day-old rats but not in younger rats. In a second experiment, anticholinergic potentiation of adrenergic arousal was observed in 25 but not 15-day-old animals. It is concluded that a cholinergic inhibitory mechanism develops gradually 15 to 25 days postnatally in the rat. 22 references. (Author abstract)

63838 $03
AUTHORS: Randall, L. O.; Scheckel, C. L.; Pool, W.
ADDRESS: Department of Pharmacology, Research Division, Hoffmann-La Roche, Inc., Nutley, New Jersey 07110
TITLE: Pharmacology of medazepam and metabolites.
SOURCE: Archives internationales de Pharmacodynamie et de Therapie (Gand).
SOURCEID: 185(1):135-148, 1970.

The pharmacological profile has been studied of the six major metabolites of medazepam which were identified in the blood and urine of human subjects, dogs and rats. N-demethylation and dehydrogenation of medazepam did not cause much change in the sedative, muscle relaxant and anticonvulsant activities in mice and cats. Diazepam, a major metabolite in man and rat, showed increased potency in these tests. Hydroxylation of diazepam in the 3 position did not cause loss of activity but N-demethylation induced considerable loss of activity and N-demethylation plus 3 hydroxylation caused further loss of activity. No significant analgesic or antiinflammatory activity was observed in mice or rats but antimorphine activity was observed. Conditioning studies in rats and monkeys suggest that medazepam has only sedative properties but some metabolites have stimulant effects at low doses and sedative effects at higher doses. 37 references. (author abstract)

63841
AUTHORS: Schallek, W.; Kovacs, J.; Kuehn, A.; Thomas, J.
ADDRESS: Department of Pharmacology, Research Division, Hoffmann-La Roche Inc., Nutley, New Jersey 07110
TITLE: Some observations on the neuropharmacology of medazepam hydrochloride (Ro 5-4556).
SOURCE: Archives internationales de Pharmacodynamie et de Therapie (Gand).
SOURCEID: 185(1):149-158, 1970.

The effects of medazepam hydrochloride on the central nervous system of the cat were studied. No significant effect on either threshold or duration of after discharges in cortex or hippocampus of immobilized cats was noted. Power spectrum analysis showed that the drug (20mg/kg, i.v.) produced a shift towards faster frequencies in spontaneous electrical activity in the caudate nucleus and hippocampus of immobilized cats. The drug (12mg/kg, p.o.) produced sedation and ataxia in freely moving cats. There was an increase in the threshold for behavioral arousal induced by electrical stimulation of the amygdala, with little or no change in the threshold of the reticular formation. There was a biphasic action on the electrocorticogram, slow waves being evident 2 hours after drug administration, while faster frequencies were dominant 4 hours after the drug. 10 references. (author abstract modified)d

63849
AUTHORS: Roll, Susan Kushner.
ADDRESS: Department of Psychology, University of California, San Diego, California
TITLE: Intracranial self-stimulation and wakefulness: effect of manipulating ambient brain catecholamines.
SOURCE: Science.
SOURCEID: 168(3937):1370-1372, 1970.

To determine if norepinephrine is a transmitter for motivation in electrical stimulation of the brain, adult male Simonsen Sprague-Dawley rats were given disulfiram, an inhibitor of norepinephrine biosynthesis. The animals had previously been implanted with stereotaxically placed tygon insulated stainless steel electrodes and had been trained to stimulate themselves by pressing a bar in a modified Skinner apparatus. Animals given the drug paused in bar pressing, appearing asleep or sedated; if replaced on the bar, they always resumed pressing at normal rates. It appears that norepinephrine is not the neurohumoral transmitter for reward in intracranial self-stimulation, since neither decreases after disulfiram nor increases in norepinephrine concentration in the brain (after chlorphentermine hydrochloride) consistently affect the rate of bar pressing at the threshold if the animal is kept awake. Studies which claim to show this effectare best accounted for by variations in wakefulness and activitylevel, either as a result of direct drug action or as a secondary result of toxicity. 8 references. (author abstract modified)

64178
AUTHORS: Orsingher, O. A.; Fulginiti, Susana.
ADDRESS: Instituto de Ciencias Quimicas, Estafeta 32, Cordoba, Argentina
TITLE: Effects of cannabis sativa on learning in rats.
SOURCE: Pharmacology (Basel).
SOURCEID: 3(6):337-344, 1970.

The effect of different schedules of treatment with a Cannabis sativa extract on several parameters of learning in the rat were studied. The parameters included acquisition of an avoidance conditioned response in a shuttlebox, performance of a previously learned response in the same box, and learning in a Lashley III maze. The action of the extract on learning routines involving different motivation and different cerebral mechanisms was compared. It was found that a single 10mg/kg dose of an extract Cannabis sativa had no

effect on the acquisition of an avoidance response in a shuttlebox; the same dose injected chronically (23 days interrupted the day before the acquisition's session) showed a depressor effect. The drug had a deconditioning effect at doses of 25 and 50mg/kg when the conditioned stimulus was a buzzer; with a light the effect was more evident even with a lower dose (10mg/kg). The performance on a Lashley III maze was also depressed by Cannabis (10mg/kg daily). 10 references. (author abstract modified)

64181
AUTHORS: Robichaud, R. C.; Gylys, J. A.; Sledge, K. L.; Hillyard, I. W.
ADDRESS: Department of Pharmacology, Warner-Lambert Research Institute, 170 Tabor Road, Morris Plains, New Jersey 07950
TITLE: The pharmacology of prazepam: a new benzodiazepine derivative.
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (Gand).
SOURCEID: 185(2):213-227, 1970.

The pharmacology of prazepam, the cyclopropylmethyl analogue of diazepam, was studied. Mice, rats, dogs and monkeys were used as experimental subjects. It was found that prazepam caused sedation, but not hypnosis in unanesthetized laboratory animals. This compound had an ED50 of 27mg/kg p.o. in the prevention of fight in isolated mice, but oral doses up to 2000mg/kg failed to cause a loss of righting reflex. In an approach - avoidance situation ("Geller's Conflict"), prazepam was effective in reducing the suppressed behavior during "conflict" periods in rats. In addition, prazepam appeared less likely to disrupt temporal discrimination in cats (fixed interval schedule) than other minor tranquilizers. Although prazepam caused convulsions when given intravenously, it had broad spectrum anticonvulsant properties comparable in potency to other benzodiazepines. Prazepam was selective in antagonizing the excitation caused by reserpine in mice pretreated with a MAO inhibitor. No significant autonomic or untoward cardiovascular effects were noted. Prazepam appears to be a useful psychotherapeutic agent with possiblyfewer side effects than observed with other members of this class. 16 references. (author abstract modified)

64253
AUTHORS: Sanghvi, I.; Gershon, S.
ADDRESS: Department of Psychiatry, New York University School of Medicine, 550 First Avenue, New York, New York 10016
TITLE: Similarities between behavioral and pharmacological actions of yohimbine and 5-hydroxytryptophan in the conscious dog.
SOURCE: European Journal of Pharmacology (Amsterdam).
SOURCEID: 11(2):125-129, 1970.

Behavioral and cardiovascular effects of 5-hydroxytryptophan (5-HTP) and yohimbine hydrochloride were compared on conscious dogs. Drugs were administered intravenously through an indwelling cannula placed in the cubital vein. The changes in blood pressure and behavior were recorded on an Offner Dynograph and a behavior rating scale. Both agents produced a marked rise in blood pressure and changes in behavior. Behavioral changes included increased restlessness, anxiety, tremors, and whining. They were found to be synergistic in these effects. Imipramine potentiated the effects of yohimbine and 5-HTP. Methysergide, brom-LSD (BOL-148) and cyproheptadine failed to reduce or prevent their effects. The data suggest that yohimbine and 5 -hydroxytryptophan may exert their action through stimulation of the same type of receptors. 16 references. (author abstract modified)

64259
AUTHORS: Geyer, Harry M., III; Watzman, Nathan; Buckley, Joseph P.
ADDRESS: Department of Pharmacology, School of Pharmacy, University of Pittsburgh, Pittsburgh, Pennsylvania 15213

TITLE: Effects of a tranquilizer and two antidepressants on learned and unlearned behaviors.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(7):964-968, 1970.

The dose response effects of chlorpromazine, imipramine, and thiazesim were investigated on unlearned behaviors (spontaneous motor activity, eating, drinking, mouse killing, self-grooming, and forced motor activity) and learned behavior using the rat pole climbing unit. Three or 4 doses of each drug were used in the study of each parameter, and ED50 values were calculated from the generated log dose response line. Ratios of the forced motor activity ED50 divided by the ED50's of the various behavioral tests were used to determine whether the blockades of the behavioral parameters occurred at debilitating or nondebilitating doses. The tranquilizer, chlorpromazine, required a debilitating dose to block 4 of the 5 unlearned behaviors. The antidepressant, imipramine, disrupted 3 of these at nondebilitating doses; the antidepressant, thiazesim, blocked all unlearned behaviors at nondebilitating doses. All compounds required debilitating doses to block the learned behavior, a conditioned avoidance response. The results generally support the hypothesis that antidepressants selectively block unlearned behaviors which are not blocked by tranquilizers until debilitating doses are used. 20 references. (author abstract)

64260
AUTHORS: Cole, Henry F.; Wolf, Harold H.
ADDRESS: College of Pharmacy, University of Missouri, Kansas City, Missouri 64110
TITLE: Laboratory evaluation of aggressive behavior of the grasshopper mouse (Onychomys).
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(7):969-971, 1970.

The genetically predisposed aggressive behavior of two species of grasshopper mouse, Onychomys leucogaster and O. torridus, was evaluated in an experimental paradigm involving isolation induced aggression. O. leucogaster exhibited considerably more aggression than did O. torridus. When aggression was provoked in Onychomys by isolation, the behavior could not be suppressed by pentobarbital nor by chlordiazepoxide. Indeed, chlordiazepoxide increased the amount of time spent fighting. Chlorpromazine was able to depress fighting behavior in torridus but not in leucogaster. The results obtained support the contention that an animal's behavioral predisposition may markedly alter the organism's response to drugs. 16 references. (author abstract)

64289
AUTHORS: Shillito, Elizabeth E.
ADDRESS: Agricultural Research Council Institute of Animal Physiology, Babraham, Cambridge, England
TITLE: A method for investigating the effects of drugs on the exploratory behaviour of mice.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 40(1):113-123, 1970.

Exploratory behavior in treated and untreated mice was observed when the animals were put on a wooden board to which 12 tunnels were fixed. The number of different tunnels entered (indicating exploration) and the total entries into tunnels were recorded over 5 min on 2 successive days. Untreated mice entered more different tunnels in the first minute on the second day on the tunnel board, and this difference in behavior was taken as an indication that exploration had occurred on the first day. When the behavior of the treated mice on the second day was similar to that of inexperienced mice on the first day it was inferred that drug treatment had adversely affected exploration. Haloperidol 4mg/kg, chlorpromazine 8mg/kg and thioridazine 16mg/kg adversely affected exploration at doses which almost immobilized the mice. Amphetamine at 8mg/kg

disrupted exploratory behavior in the mice, although the mice were observed to move round the board very quickly. With tranylcypromine 2mg and nialamide 100mg, increased exploratory behavior by comparison with controls was recorded in the mice when they were tested 24 hr after drug treatment. Imipramine at 20mg/kg reduced the total number of tunnels entered by the mice on the first day, but on the second day the mice behaved in a similar way to mice treated with monoamine oxidase inhibitors. 12 references. (author abstract modified)

64333
AUTHORS: Vakhing, V. A.; Allikmets, L. Kh.
ADDRESS: Department of Psychiatry and Central Medical Research Laboratory, Tartu University, Tartu, Estonia, U.S.S.R.
TRTITLE: /Behavioral and visceral reactions elicited by chemical stimulation of the hypothalamus and septum in cats./
TITLE: Povedencheskiye i vegetativnyye reaktsii, vyzvannyye khimicheskoy stimulyatsiyey gipotalamusa i septuma.
SOURCE: Fiziologicheskii Zhurnal SSSR imeni I. M. Sechenova (Moskva).
SOURCEID: 56(1):38-47, 1970.

In experiments on 46 cats in a free behavior situation, the effects of microinjection of acetylcholine, noradrenaline and serotonin into the hypothalamic, preoptic and septal regions were investigated. Emotional - affective reactions of a negative nature were elicited only by acetylcholine injected into the hypothalamus. After microinjection of acetylcholine into the lateral septal and dorsal preoptic regions, behavioral inhibition and sleep occurred. Visceral (autonomic) reactions were elicited by both acetylcholine and serotonin microinjections into all brain structures investigated. Behavioral and visceral effects of noradrenaline were significantly weaker than those of acetylcholine and serotonin. Preliminary intramuscular or intracerebral injection of benactyzine, imipramine and amitriptyline decreased or blocked the effects of acetylcholine. Imipramine and amitriptyline intensified visceral effects of serotonin. 22 references. (author abstract modified)f

64365
AUTHORS: Rosic, N.; Bignami, G.
ADDRESS: Department of Therapeutical Chemistry, Istituto Superiore di Sanita, Rome, Italy
TITLE: Depression of two-way avoidance learning and enhancement of passive avoidance learning by small doses of physostigmine.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(4):311-316, 1970.

The effects of physostigmine on the acquisition of 2 way active avoidance and of GO - NO GO avoidance discrimination were studied in rats. The drug was without effect on active avoidance learning at the lowest dose tested (0.025mg/kg s.c.), while a significant retardation was observed after the administration of 0.05 or 0.075mg/kg. Both 0.025 and 0.05mg/kg of the drug changed the distribution of errors during the acquisition of the GO -NO GO discrimination, by increasing the frequency of active avoidance errors and decreasing the frequency of passive avoidance errors. The overall effect, in terms of total errors, was in the direction of a slight facilitation of discrimination learning, which was significant only in the second of 10 training sessions. These opposite results on active and passive avoidance learning are interpreted as showing that small doses of physostigmine enhance the activity of response inhibiting systems, without producing general changes in sensory and/or associative functions. 12 references. (author abstract)

64367
AUTHORS: Key, B. J.; White, R. P.
ADDRESS: Department of Experimental Neuropharmacology, Medical School, University of Birmingham, Birmingham 15, England

TITLE: Neuropharmacological comparison of cystathionine, cysteine, homoserine and alpha-ketobutyric acid in cats.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(4):349-357, 1970.

Overt changes in behavior and the patterns of electrocortical activity induced by cystathionine, cysteine, homoserine and alpha-ketobutyric acid administered into the lateral cerebral ventricle, were studied in 2 groups of cats. One group was used for acute studies and in all of these animals the spinal cord was sectioned at the C1 level (encephale isole preparation). This group was given all the different solutions during one experimental period. The other group consisted of chronic preparations with permanently implanted ventricular cannulae. These animals were given single injections of the various experimental solutions at 3 to 4 day intervals. In the encephale isole preparations cystathionine increased the synchrony of the electrocorticogram (ECoG) and lowered the blood pressure. In contrast, cysteine produced electrocortical desynchronization, raised the blood pressure and usually evoked activity of the facial musculature. The ECoG effects of cysteine were attenuated or blocked by cystathionine. In the chronic preparations, cysteine induced ECoG activation and markedly increased spontaneous motor activity. Cystathionine shortened the period of time to the onset of sleep. The effects of solutions of homoserine, alpha-ketobutyric acid, acidified saline and physiological saline were either absent, or equivocal. It was concluded that in the free form cystathionine, or its cleavage product cysteine, may be important in the normal functioning of the brain and play a role in the pathogenesis of certain inborn errors of metabolism independently of their importance as metabolic intermediaries. 14 references. (author abstract)

64375
AUTHORS: Gray, Jeffrey A.
ADDRESS: Institute of Experimental Psychology, Oxford, England
TITLE: The psychophysiological basis of introversion-extraversion.
SOURCE: Behaviour Research and Therapy (Oxford).
SOURCEID: 8(3):249-266, 1970.

On both psychological and physiological grounds it is suggested that the hypothesis in Eysenck's theory of introversion-extraversion attributing greater conditionability to the introvert should be replaced by the hypothesis that the introvert is relatively more sensitive to punishment and to frustrative nonreward. The data on which this conclusion is based stem chiefly from the study of eyeblink conditioning in man as a function of personality, and from the study of the physiological locus of action of the extraverting drug, sodium amobarbital, in animals. It is suggested that the physiological basis of introversion includes, besides the Ascending Reticular Activating System, an inhibitory system comprising the orbital frontal cortex, the medial septal area and the hippocampus. This system is able to carry out the essential psychological functions believed by Eysenck to underlie introversion-extraversion. A new conception of neuroticism as reflecting degree of sensitivity to both reward and punishment is also proposed. 65 references. (author abstract)

64390
AUTHORS: Blum, Kenneth.
ADDRESS: Department of Experimental Pharmacology, Southwest Foundation for Research and Education, P. O. Box 28147, San Antonio, Texas 78228
TITLE: Effects of chlordiazepoxide and pentobarbital on conflict behavior in rats.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(5):391-398, 1970.

A punishment discrimination ("conflict") was conditioned in rats by simultaneously rewarding with food (sweetened, condensed milk) and punishing with shock all lever responses made in the presence of an

auditory stimulus. Chlordiazepoxide and pentobarbital were administered in order to compare degrees of attenuation of conflict behavior relative to the production of behavioral debilitation. Chlordiazepoxide produced the maximum attenuation at doses that produced only minimum debilitation. In general, conflict attenuation ("antianxiety") was greater under chlordiazepoxide while general debilitation (behavioral toxicity) was greater for pentobarbital. 17 references. (author abstract)

64392
AUTHORS: Bapna, J. S.; Dandiya, P. C.
ADDRESS: Department of Pharmacology, S.M.S. Medical College, Jaipur, India
TITLE: Modification of the effects of antipsychotic agents on the "open field" performance of rats by treatment with alpha-methyl tyrosine or p-chlorophenylalanine.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(5):361-366, 1970.

Experiments were performed to study the effect on "Open Field" behavior of subthreshold doses of reserpine and chlorpromazine in rats with lowered brain catecholamine or 5-hydroxytryptamine levels. The doses of alpha-methyltyrosine which are known to lower brain catecholamine contents by 65 percent remarkably enhanced the effects of antipsychotic agents on ambulation and rearing responses. These effects could be partially antagonized by simultaneous administration of L-DOPA. The lowering of 5-hydroxytryptamine to the extent of 90 percent by p-chlorophenylalanine failed to modify the effects of these antipsychotic agents. The findings suggest that the brain catecholamines levels play a greater role in the mechanism of antipsychotic agents as compared to 5-hydroxytryptamine levels. 18 references. (author abstract)

64407
AUTHORS: Johnson, P. N.
ADDRESS: Department of Psychology, University of Birmingham, P.O. Box 363, Birmingham 15, England
TITLE: The effects of chlorpromazine on one-trial passive avoidance learning in mice: further examination of pre- and post-learning administration.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):11-18, 1970.

An attempt was made (1) to replicate the effects of postlearning chlorpromazine injections and (2) to examine a further series of prelearning and postlearning injection times to provide more information about the time course of the drug's action and of the memory process associated with 1 trial passive avoidance learning. Chlorpromazine in doses of 0.5mg/kg was administered to mice 0.5, 2, or 10 min after a 1-trial passive avoidance learning experience. The drug produced effects on the magnitude and rate of extinction of the learned response dependent upon the injection time, confirming results contained in an earlier report. In a second experiment with doses of 2.0mg/kg, the effects of further injection times were investigated. The drug had no effect when given 240 min before learning, but produced maximal blocking of response acquisition when given 120 and 8 min before learning. Drug injections 6 and 3 min before learning were suggested as having actions on postlearning memory traces. A distinction was noted between the effects of drug injections 1 and 1.5 min after learning and this was related to an effect on a rapidly decaying short-term memory trace. Chlorpromazine had no effect when given 20 min after learning. 5 references. (author abstract modified)

64410
AUTHORS: Heise, George A.; Lilie, Nellie L.
ADDRESS: Department of Psychology, Indiana University, Bloomington, Indiana 47401

TITLE: Effects of scopolamine, atropine, and d-amphetamine on internal and external control of responding on non-reinforced trials.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):38-49, 1970.

The effects of scopolamine, atropine, and d-amphetamine on internally and externally controlled nonresponding were compared in an experimental situation where the present and recent stimuli that control the rat's behavior were more explicitly defined than in a reinforcement withdrawal experiment. Rats learned not to respond on nonreinforced trials in a discrete trial situation in which trial responses were reinforced only if preceded by 3 or more nonresponse trials. Drug effects were measured: 1) when the same external stimuli were present on all trials and trial responding was therefore controlled by events that occurred prior to the trial ("internal control"); and 2) when the external stimuli on trials on which responding was reinforced were different from the external stimuli present on trials on which responding was not reinforced ("external control"). Scopolamine impaired performance (i.e. reduced the percentage of trial responses that were reinforced) to about the same extent under the internal and external control conditions. d-Amphetamine, on the other hand, impaired nonresponding on trials only under internal control conditions. Atropine affected both internally and externally controlled nonresponding but had a greater effect on internally controlled nonresponding. 6 references. (author abstract modified)

64412
AUTHORS: Schneider, Allen M.; Kapp, Bruce S.; Sherman, William M.
ADDRESS: Department of Psychology, New York University, University Heights, Bronx, New York 10453
TITLE: The effects of centrally and peripherally acting cholinergic drugs on the short-term performance gradient following passive-avoidance training.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):77-81, 1970.

Rats, injected with physostigmine salicylate, neostigmine methylsulfate, atropine sulfate, atropine methylate, or saline, were trained in a passive avoidance platform procedure and were tested 5, 15, or 120 sec later. In the saline treated groups step down latencies increased between the 5 second and 15 second intervals andstabilized between the 15 second and 120 second intervals. Relative to saline controls, the drugs had the following effects: physostigmine decreased test latencies at the 15 and 120 second intervals; atropine sulfate and methylate increased test latenciesat the 5 second interval; neostigmine did not modify test latencies at any of the 3 intervals. 9 references. (author abstract)

64414
AUTHORS: Srimal, R. C.; Dhawan, B. N.
ADDRESS: Pharmacology Division, Central Drug Research Institute, Chattar Manzil Palace, Lucknow-1, India
TITLE: An analysis of methylphenidate induced gnawing in guinea pigs.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):99-107, 1970.

Twenty compounds acting on the central nervous system and the autonomic nervous system were tested in guinea pigs for their ability to induce gnawing. Only methylphenidate induced vigorous gnawing similar to that produced by apomorphine and amphetamine. Methylphenidate differs in its mode of action from both apomorphine and amphetamine. In the guinea pig, phenylethyl configuration with OH groups at para and meta positions of the phenyl ring does not seem to be an essential criterion for inducing gnawing as suggested for the rat (Ernst, 1965). Catecholamines do not appear to play any

significant role in the mediation of methylphenidate gnawing, or even in the gnawing response itself in guinea pigs, since increase in the level of dopamine and other catecholamines does not induce gnawing. 12 references. (author abstract)

64415
AUTHORS: Merlo, Alicia B.; Kuzniecki, Nelida.
ADDRESS: Catedra de Farmacologia Experimental, Facultad de Farmacia y Bioquimica, Junin 956, Buenos Aires, Argentina
TITLE: Effect of imipramine and chlorimipramine on an acute instrumental trace conditioned reflex in rats.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):124-128, 1970.

An acute conditioned trace reflex was established in rats using a buzzer (5 sec) as a conditioned stimulus, and an electric shock (2.5 mA, 50 cycles per second) as an absolute stimulus. The latter lasted for 1 second and was applied through the grid floor of the training box. The traces (time intervals between the end of the conditioned stimulus and the initiation of the absolute stimulus) were 0, 2 and 10 sec for the different control groups and for those treated with imipramine and chlorimipramine. A conditioned response was considered positive when the animal, in order to avoid the absolute stimulus, lifted 1 or both forelegs during the buzzer or the corresponding trace interval. The number of conditioned responses was significantly lower in the 0 trace control group than in the control groups trained with longer traces. Imipramine and chlorimipramine (10mg/kg) were administered by intraperitoneal injection 5 min before the conditioning session. Both drugs significantly decreased the number of conditioned responses to all traces studied up to the same level. This shows that these drugs not only impaired acquisition, but also annulled the influence of trace duration upon it. 13 references. (author abstract)

64417
AUTHORS: Carlini, E. A.; Santos, M.; Claussen, U.; Bieniek, D.; Korte, F.
ADDRESS: Faculdade de Ciencias Medicas da Santa Casa, Rua Cesario Motto Jr., 112, San Paulo, Brazil
TITLE: Structure activity relationship of four tetrahydrocannabinols and the pharmacological activity of five semi-purified extracts of cannabis sativa.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):82-93, 1970.

The structure activity relationships of 4 tetrahydrocannabinols (THC) and the pharmacological activity of 5 semipurified extracts from Cannabis sativa were studied using 4 biological methods: corneal areflexia in rabbits (Gayer test) and catatonia, decrease of motor activity and suppression of isolation induced aggressiveness in mice. Modifications in the structure of pure, natural delta-9-THC rendered the resultant compounds inactive only when activity was measured by the Gayer test; by the other 3 methods the activity ranged from 0.20 to equal to the activity of pure delta-9-THC. It was concluded that of the methods employed, the Gayer test was the only useful procedure to measure delta-9-THC content in mixtures. This was confirmed by the relationship found between delta-9-THC content and activity using five semipurified extracts. 13 references. (author abstract)

64424
AUTHORS: Kubena, Robert K.; Barry, Herbert, III.
ADDRESS: Department of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania 15213
TITLE: Interactions of delta 1-tetrahydrocannabinol with barbiturates and methamphetamine.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):94-100, 1970.

Male albino rats were tested for interactions of delta-1-tetrahydrocannabinol (delta-1-THC), thought to be the principal euphoric constituent of marihuana, with the depressant action of 2 barbiturates and with the stimulant action of methamphetamine. In a test of spontaneous motor activity in a photocell arena, delta-1-THC (4mg/kg and 16mg/kg) potentiated the depressant effects of both pentobarbital (10mg/kg) and barbital (120mg/kg) and prolonged sleeping time under pentobarbital (30mg/kg) and barbital (240mg/kg). Since barbital was not metabolized, interaction with delta-1-THC was attributable to synergetic depressant actions in the central nervous system rather than to inhibition of microsomal enzymes. The higher dose of delta-1-THC (16mg/kg), which by itself greatly decreased spontaneous motor activity, failed to diminish the stimulant activity of 2 doses of methamphetamine (0.5mg/kg and 2mg/kg). The percentage of animals surviving a toxic dose of methamphetamine (25mg/kg) was increased by delta-1-THC (4mg/kg and 16mg/kg). Thus, delta-1-THC has sedative or tranquilizing actions, enhancing depressant effects of barbiturates and counteracting toxic effects of methamphetamine stimulation. These drug interactions were found even with a low dose of delta-1-THC (4mg/kg), which by itself had little effect on spontaneous motor activity. 22 references. (author abstract modified)

64426
AUTHORS: Hanson, H. M.; Stone, C. A.; Witoslawski, J. J.
ADDRESS: Merck Institute for Therapeutic Research, West Point, Pennsylvania 19486
TITLE: Antagonism of the antiavoidance effects of various agents by anticholinergic drugs.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):117-124, 1970.

The antiavoidance activity of chlorpromazine, trifluoperazine, perphenazine, thioridazine, haloperidol, ethomoxane, chlorprothixene, tetrabenazine and reserpine in squirrel monkeys was found to be significantly reduced when administered with a concurrent dose of benztropine. In contrast, the antiavoidance activity of chlordiazepoxide, pentobarbital, meprobamate, chloral hydrate and paraldehyde was either unaffected or increased by concurrent benztropine administration. Benztropine, scopolamine, cyproheptadine, atropine and trihexyphenidyl reversed the antiavoidance activity of a standard dose of perphenazine. The peripheral anticholinergic actions of these compounds as measured by pupil dilatation were not found to be highly correlated with their action upon avoidance activity, this being due to a difference in central versus peripheral anticholinergic potency. In Macaca speciosa, the antiavoidance action of perphenazine could be reversed by the i.v. injection of benztropine. Thus, the main effect seen was not due to inhibition of absorption, but to a pharmacologic interaction of the compounds studied. Reversal of the antiavoidance activity of major tranquilizing compounds by anticholinergics may be useful in distinguishing these compounds from other types of depressants. 19 references. (author abstract modified)

64475
AUTHORS: Stolerman, I. P.; Kumar, R.
ADDRESS: Department of Pharmacology, University College London, Gower Street, London W. C. 1, England
TITLE: Preferences for morphine in rats: validation of an experimental model of dependence.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(2)"137-150, 1970.

Rats were induced to administer morphine to themselves by drinking solutions of it in preference to water; this behavior was found to be a valid model of morphine dependence. Previous passive medication with morphine was not necessary; initial aversions for the bitter morphine solutions were converted into preferences after the rats were repeatedly given only morphine solutions to drink in order

to relieve thirst. The consumption of solutions of quinine, which were initially equally aversive, did not increase, suggesting that the repeated pairing of a bitter taste with relief of thirst did not account for the preference for the morphine solutions. The post-ingestional effects of morphine thus provided primary reinforcement for the rats; they were able to regulate their daily intake of the drug after being injected with varying doses of it and they lost weight abruptly during enforced abstinence. There was also evidence that the bitter taste of morphine had become a secondary reinforcer for rats with established preferences. 23 references. (author abstract)

64476
AUTHORS: Niemegeers, C. J. E.; Verbruggen, F. J.; Janssen, P. A. J.
ADDRESS: Janssen Pharmaceutica, B-2340 Beerse, Belgium
TITLE: The influence of various neuroleptic drugs on shock avoidance responding in rats. III. Amphetamine antagonism in the discriminated Sidman avoidance procedure.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(2):151-159, 1970.

The inhibitory effects of 4 neuroleptic drugs on amphetamine induced stimulation in a discriminated Sidman avoidance procedure in rats were measured. Amphetamine, 0.63mg/kg s.c. increased responses and decreased warning stimuli, warning responses and shock. Relatively low doses of all 4 neuroleptics antagonized the amphetamine induced changes. The order of potency was haloperidol which was greater than pimozide which was greater than chlorpromazine which was greater than pipamperone. The duration of action was pimozide which was greater than haloperidol which was greater than pipamperone which was greater than chlorpromazine. Haloperidol, pimozide and pipamperone restored the amphetamine induced changes to the initial control levels in the order: shocks, warning stimuli, warning responses and responses. With chlorpromazine this order was reversed, except for responses. The different pharmacological profiles of haloperidol, pimozide and pipamperone were discussed. 12 references. (author abstract)

64479
AUTHORS: Thompson, T.; Trombley, J.; Luke, D.; Lott, D.
ADDRESS: Department of Psychiatry, University of Minnesota Medical School, Minneapolis, Minnesota 55455
TITLE: Effects of morphine on behavior maintained by four simple food-reinforcement schedules.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(2):182-192, 1970.

The effects of morphine on behavior maintained by 4 simple food reinforcement schedules were studied. Twelve rats, conditioned on 3 values of fixed ratio, variable ratio, fixed interval and variable interval food reinforcement schedules, were administered 1.0, 3.0 and 6.0mg/kg i.p. of morphine or saline. Overall response rate varied with schedule, schedule value and morphine dose. The effect of morphine on overall rate varied with the baseline saline rate generated by the schedules, and the relative rate change also varied with the type of schedule. 13 references. (author abstract modified)

64481
AUTHORS: Layden, Thomas A.; McGrath, W. Robert; Smith, Fellner D.
ADDRESS: Schick Pharmaceutical, Inc., 12001 Ambaum Boulevard, S. W., Seattle, Washington 98146
TITLE: Psychopharmacological action of nicotinamide adenine dinucleotide.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(2):198-202, 1970.

The effect of nicotinamide adenine dinucleotide upon the response rates in variable interval and Sidman avoidance schedules was studied in rats. Bar pressing on the variable interval reinforcement schedule was significantly reduced during the 15 min following the administration of 10mg/kg i.p. and during the 60 min following the administration of 30mg/kg nicotinamide adenine dinucleotide. Response rates on the Sidman avoidance schedule were significantly reduced during the 60 min following the administration of 100mg/kg nicotinamide adenine dinucleotide. 11 references. (author abstract)

64499
AUTHORS: Siegel, Ronald K.
ADDRESS: Department of Psychology, Dalhousie University, Halifax, Nova Scotia, Canada
TITLE: Effects of cannabis sativa and LSD on pigeons in three visual environments.
SOURCE: Perceptual and Motor Skills.
SOURCEID: 30(2):510, 1970.

The effects of cannabis sativa extracts and LSD on the number of color changes reported by pigeons in a standard visual display is reported. Six groups of pigeons were trained to peck at either presence or absence of random "psychodelic" color slides, random projected lights or were given non-differential training with white light. Cannabis (30mg/kg in 95% ethanol) was found to reduce responses in blank trials whereas LSD (500 micrograms/kg) increased responding and 95% ethanol was found to exert no effect. reference.

64590
AUTHORS: Moore, Kenneth E.
ADDRESS: Department of Pharmacology, Michigan State University, East Lansing, Michigan
TITLE: Effects of disulfiram and diethyldithiocarbamate on spontaneous locomotor activity and brain catecholamine levels in mice.
SOURCE: Biochemical Pharmacology.
SOURCEID: 18(7):1627-1634, 1970.

To examine the behavioral consequences of depleting the brain of only norepinephrine, mice were treated with intraperitoneal injections of diethyldithiocarbamate (DDC) or disulfiram (DS) (200mg/kg), both of which inhibit dopamine-beta-hydroxylase. Neither altered brain levels of dopamine but caused a dose dependent reduction of both the brain content of norepinephrine and the spontaneous locomotor activity of mice. These latter effects were not causally related, since pretreatment with a monoamine oxidase inhibitor prevented the DDC and DS induced depletion of norepinephrine but did not alter the ability of these drugs to depress spontaneous locomotor activity. Exposure of the mice to a 4 degree environment did not alter DS induced depletion of brain norepinephrine or behavioral depression. When administered in the diet, DS reduced the brain content of norepinephrine but did not depress motor activity; DDC did not alter either parameter. The central depressant effects of DDC and DS are not exclusively due to the ability of these drugs to alter the absolute levels of brain catecholamines. 23 references. (author abstract modified)

63617
AUTHORS: Matsuhiro, Betty; Furst, Arthur.
ADDRESS: Institute of Chemical Biology, University of San Francisco, San Francisco, California 94117
TITLE: 2,3,6-Trimethoxynitrostyrene and its beta-phenethylamine.
SOURCE: Journal of Medicinal Chemistry.
SOURCEID: 13:973, 1970.

It is doubted that the 2,3,6-trimethoxyphenethylamine reported in the literature as having no activity on the presence of soluble amine oxidase from rabbit liver was the correct compound. To test that belief, 2,3,6-trimethoxybenzaldehyde was prepared by a different method. Condensing the substituted aldehyde with methyl nitrite resulted in a crystalline substituted nitrostyrene. The compound and its beta-phenethylamine produced hypomotility in a 20 g mouse when administered as a saline solution at 16mg/kg. At 31mg/kg the compound incuded fatal convulsions. A test using homogenized mouse brain showed that this compound is either a competitive substrate for the monoamine oxidase or an inhibitor of that enzyme. 6 references.

64143
AUTHORS: Escalante, O. Duarte; Ellinwood, Everett H., Jr.
ADDRESS: Department of Psychiatry, Duke University Medical Center, Durham, North Carolina 27706
TITLE: Central nervous system cytopathological changes in cats with chronic Methedrine intoxication.
SOURCE: Brain Research (Amsterdam).
SOURCEID: 21(1):151-155, 1970.

Histochemical and cytopathological central nervous system changes associated with chronic Methedrine intoxication are reported. Five cats received initial daily intramuscular doses of 20mg/kg Methedrine which was gradually increased to 50mg/kg for 14 days. The animals were then sacrificed and the brain prepared for histological investigation by hematoxylin and eosin staining, catecholamine fluorescence and acetylcholinesterase reaction techniques. Enlarged neurons from the medulla oblongata and lower pons were observed in the intoxicated cats. These cells had diameters greater than 100 microns and were irregular in shape. Nissl material was arranged in clusters of large granules; the nuclei were eccentric and an absence of monoamine fluorescence was apparent in cells from these areas. Cholinesterase enzyme activity was increased substantially in cells from the medulla oblongata, pons, mesencephalon and diencephalon. Catecholamine depletion may be a mediator of chromatolysis in amphetamine intoxication. 10 references.

64160
AUTHORS: Wiberg, G. S.; Coldwell, B. B. Trenholm, H. L.
ADDRESS: Pathology and Toxicology Section, Research Laboratories, Food and Drug Directorate, Ottawa, Ontario, Canada
TITLE: Toxicity of ethanol barbiturate mixtures.
SOURCE: Journal of Pharmacy and Pharmacology (London).
SOURCEID: 22(6):465, 1970.

A letter to the editor is presented concerning the toxicity of ethanol - barbiturate mixtures. In continuing research, it has been found that: ethanol (3g/kg, i.p. in rats) with barbiturates markedly reduces blood pressure hence, urine formation and renal clearance of barbiturates; ethanol produces a dose related decrease in body temperature which would decrease hepatic metabolism of barbiturate and ethanol; ethanol depresses respiration rate and lowers the blood pO2 levels, which would reduce ethanol and barbiturate metabolism; pentobarbitone enhances activity of purified rat liver alcohol dehydrogenase, but retards metabolism by liver slices; ethanol is more toxic in older rats and there is an increased sensitivity to ethanol -barbiturate mixtures; and ethanol alters the distribution of barbiturates in body compartments. The inherent dangers associated with combined use of ethanol and barbiturates must be emphasized for the general public. 7 references.

64277
AUTHORS: Horita, A.; Carino, M. A.
ADDRESS: Department of Pharmacology, School of Medicine, University of Washington, Seattle, Washington
TITLE: Modification of the toxic actions of l-tryptophan by pargyline and p-chlorophenylalanine.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(4):1521-1524, 1970.

The role of 5-hydroxytryptamine metabolite of l-tryptophan inthe toxicity produced by this amino acid was investigated in the presence of p-chlorophenylalanine and pargyline in male Sprague-Dawley rats. Pretreatment with p-chlorophenylalanine (200-300mg/kg, i.p.) did not significantly alter the tryptophan toxicity, pargyline (25mg/kg, i.p.) reduced the LD50 of tryptophan from 12 to 2mmoles/kg, i.p., and a combination of the 2 resulted in a protection to the challenge with tryptophan. Brain levels of 5-hydroxytryptamine (microgram/g) stood at 0.48 for controls, 0.78 in animals after 12mmoles/kg tryptophan, 0.19 to 0.28 in animals after p-chlorophenylalanine with 12mmoles/kg tryptophan, 1.15 to 1.40 in animals after pargyline with 2 to 4mmoles/kg tryptophan, and 0.75 to 1.22 in animals after p-chlorophenylalanine and pargyline with 8 to 12mmoles/kg tryptophan. Apparently 5-hydroxytryptamine is related to the toxicity of tryptophan in p-chlorophenylalanine and pargyline treated rats, but the total brain levels do not correlate with the toxicity. 6 references.

64315
AUTHORS: Kato, T.; Jarvik, L. F.; Roizin, L.; Moralishvili, E.
ADDRESS: Department of Medical Genetics, New York State Psychiatric Institute, New York, New York
TITLE: Chromosome studies in pregnant Rhesus macaque given LSD-25.
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(4):245-250, 1970.

The effects of LSD on the chromosomes of pregnant Rhesus monkeys and their offspring was studied. Injection of LSD in doses ranging from 0.125 to 1.0mg/kg was associated with a transient increase in chromosome breaks in 3 of the 4 experimental monkeys. One of the 2 control animals showed a rise in break frequency similar to that of one of the experimental animals. The highest frequency of breaks (12%) was twice the highest control value (6%). There was a large variation in chromosome breaks in one control (0 to 6%) and there were also diverse intervals between the last LSD treatment and the first post-drug leukocyte culture (4 to 15 days). This experiment was designed as a pilot study to provide directions for future research rather than definitive answers to questions regarding the potential of LSD for genetic damage. 31 references.

64422
AUTHORS: Alexander, George J.; Gold, George M.; Miles, Bruno E.; Alexander, Rita B.
ADDRESS: 722 West 168th Street, New York, New York 10032
TITLE: Lysergic acid diethylamide intake in pregnancy: fetal damage in rats.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):48-59, 1970.

Oral or subcutaneous administration of LSD to hundreds of pregnant rats resulted in damage to litters which was 3 to 4 times higher than in corresponding controls given distilled water or saline. The proportion of deaths during gestation, abortions, resorptions, runting, offspring stillbirths and the rate of offspring mortality was increased. No unusual number of specific deformities was encountered. Teratogenicity during any particular organogenetic period was not demonstrated. Treatment during the first 7 days was found harmful; treatment later in pregnancy was ineffective. The LSD effects appeared to be dose related and persisted into the second generation. 20 references. (author abstract)

63725
AUTHORS: Stretch, Roger; Gerber, Gary J.
ADDRESS: Department of Psychology, University of Western Ontario, London 72, Ontario, Canada
TITLE: A method for chronic intravenous drug administration in squirrel monkeys.
SOURCE: Canadian Journal of Physiology and Pharmacology (Ottawa).
SOURCEID: 48(8):575-581, 1970.

A system for the infusion of drug solutions into the blood stream of relatively unrestrained and unanesthetized squirrel monkeys, via a chronic intravenous catheter is described. The system is used in conjunction with free operant conditioning procedures to investigate behaviors associated with drug self-administration. The technique involves several modifications of previously used procedures, allowing the investigator to disconnect the infusion apparatus and release the monkey from a restraint device following each daily period of experimentation. The method is described with reference to cannula construction, the cannula protection and infusion delivery system, the fluid reservoir and pump, surgical procedures, and behavioral testing procedures. Representative data, pertaining to the maintenance of schedule-controlled behavior by response-contingent infusions of d-amphetamine sulfate, are described to illustrate a specific application of the technique. 11 references.

63848
AUTHORS: Spector, Sydney; Parker, Charles W.
ADDRESS: Roche Institute of Molecular Biology, Nutley, New Jersey 17110
TITLE: Morphine: radioimmunoassay.
SOURCE: Science.
SOURCEID: 168(3937):1347-1348, 1970.

A radioimmunoassay for morphine was developed using, as hapten, morphine which was made antigenic by coupling to a protein at the phenolic group of the molecule. First, morphine was converted to 3-O-carboxymethylmorphine, and this was coupled to bovine serum albumin (BSA) in aqueous solution in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide. Conjugates contained three to four carboxymethylmorphine groups per molecule of BSA. Rabbits were immunized with the protein - morphine conjugate and given booster injections every six to eight weeks. Incubation of antiserum obtained from immunized rabbits with 3H-dihydromorphine produced precipitates containing radioactive antibody - bound dihydromorphine. Extremely low concentrations of morphine (0.5ng) could be measured with the procedure. Nalorphine decreased precipitation of radioactivity by about 35 percent; the same amount of methadone produced little or no inhibition. It is not yet known whether morphine antibodies may interfere with the pharmacological effects of morphine. 8 references.

63989
AUTHORS: Bartonicek, V. J.
ADDRESS: Sanct Lars Hospital, Lund, Sweden
TITLE: Special application of fluorescence histochemistry: studies on eight monoamine oxidase inhibitors in brain neurons.
SOURCE: Pharmacology (Basel).
SOURCEID: 4(1):16-24, 1970.

Eight monoamine oxidase (MAO) inhibitors of alkylhydrazine, alkylamine and butyrophenone types including tranylcypromine, pheniprazine, isocarboxazid, phenelzine, pargyline, nialamide, gamma-morpholino-butyrophenone hydrochloride, and gamma-(3,5-dimethyl-morpholino)-butyrophenone hydrochloride were investigated. The irrelative inhibitory potency in rat brain neurons was compared

by means of fluorescence histochemistry. Each MAO inhibitor was injected into 4 rats, who were occasionally observed and their behavior registered. Four and 48 hr, and sometimes 2, 6, 12 or 24 hr following the injection the rats were decapitated. It was found that the 2 morpholino-butyrophenone compounds were characterized by a very potent, but shortlasting inhibition of MAO. Also tranylcypromine, pheniprazine, and phenelzine were stronger MAO inhibitors than isocarboxazide, nialamide and pargyline. The compounds were grouped on the basis of their potency and duration of the effect. Also pheniprazine and tranylcypromine were found to augment activity of the rats as reflected in enhanced spontaneous motility and forced responsivity to painful, acoustic and tactile stimuli. Tranylcypromine also provoked piloerection and fine frequent tremors of body musculature with higher doses. 23 references. (author abstract modified)

64002
AUTHORS: Iversen, L. L.; Jarrott, B.
ADDRESS: Department of Pharmacology, University of Cambridge, England
TITLE: Modification of an enzyme radiochemical assay procedure for noradrenaline.
SOURCE: Biochemical Pharmacology.
SOURCEID: 19(5):1841-1843, 1970.

The modification of an assay procedure for noradrenaline is described, based on the transfer of radioactively labeled methyl groups from S-adenosylmethionine to unlabeled noradrenaline, catalysed by the enzyme phenylethanolamin-N-methyl transferase. The sensitivity of the method is approximately 0.5 nanogram of L-noradrenaline. The results of determination of endogenous noradrenaline content in vas deferens, nictitating membrane, auricle, iris, and salivary glands by the enzymatic method agreed well with the values previously obtained by fluorometric assay procedures. The bovine adrenal medullary preparation of phenylethanolamin-N-methyl transferase was preferable to the rabbit preparation, offering higher sensitivity. This modification depends on measuring the complete conversion of noradrenaline to adrenaline, rather than measuring the rate of formation as done in the original procedure. Noradrenaline conversion was not inhibited by dopamine or 5-hydroxytryptamine at concentrations up to 5mcg/ml. The advantage of this method is that it allows noradrenaline to be assayed in small aliquots of tissue homogenates, leaving material for assay of other components. 4 references.

64262
AUTHORS: Murty, B. S. R.; Baxter, R. M.
ADDRESS: Faculty of Pharmacy, University of Toronto, Toronto 181, Ontario, Canada
TITLE: Spectrophotometric determination of chlorpromazine in pharmaceutical dosage forms.
SOURCE: Journal of Pharmaceutical Sciences.
SOURCEID: 59(7):1010-1011, 1970.

A rapid and convenient spectrophotometric method for the determination of chlorpromazine hydrochloride and its unit dosage forms is described. The unit forms analyzed were tablet form, injection, suppository and syrup. Extensive separation and extraction of the active ingredient were not required. The microsensitive color response with Van Urk's reagent was the basis of the analytical technique. The results were reproducible. 8 references. (author abstract modified)

06 METHODS DEVELOPMENT

64609
AUTHORS: Gettner, H. H.; Rolo, A.; Abramson, H. A.
ADDRESS: South Oaks Research Foundation, Sunrise Highway, Amityville, New York 11701
TITLE: Lysergic acid diethylamide (LSD 25): XXXIX. The effect of high temperatures on stability.
SOURCE: Journal of Psychology.
SOURCEID: 75:35-40, 1970.

Using the surfacing reaction of goldfish as a bioassay method, the effect of heat on the stability of LSD-25 was studied. Boiling 1.0 mg/ml of LSD-25 in the dark up to 4 hr did not lead to an appreciable destruction of the LSD-25. Baking the LSD-25 in a batter made from commercial Bisquick at 300 degrees F for 1 hr and freezing it for several weeks led to some destruction of the LSD-25, but atleast 50% of the LSD-25 remained active. 3 references. (author abstract)

07 EARLY CLINICAL DRUG TRIALS

64173
AUTHORS: Sternalski, M.
ADDRESS: Cracow, Poland
TRTITLE: /Lyogen in the treatment of mental diseases in children./
TITLE: Zastosovanie Lyogenu v leczeniu chorob psychicznych dzieci.
SOURCE: Przeglad Lekarski (Krakow).
SOURCEID: 26(3):403-404, 1970.

Lyogen (fluphenazine), one of the phenothiazine drugs, has been used successfully in the treatment of psychotic and schizophrenic patients; unfavorable indications were seen only infrequently. In a psychiatric study, lyogen was administered to 20 children in the Cracov Psychiatric Clinic; 17 were inpatients ranging from 4.5 to 12 years of age, and 3 were outpatients from 4 to 10 years old. The inpatients included schizophrenics, psychotics, and neuropaths. The 3 children in the ambulatory clinic suffered from neuroses and onanism. Secondary symptoms appeared in the children twice as postpyramidal effects after intramuscular administration of lyogen and once after oral administration. In addition, one child became jaundiced. 9 references.

64406
AUTHORS: Lader, M. H.; Sakalis, G.; Tansella, M.
ADDRESS: Department of Psychiatry, Institute of Psychiatry, de Crespigny Park, Denmark Hill, London S.E.5, England
TITLE: Interactions between sympathomimetic amines and a new monoamine oxidase inhibitor.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):118-123, 1970.

A relatively safe method is described for the screening of new monoamine oxidase inhibitors with respect to their potentiation of dietary and sympathomimetic amines. Clorgyline, a potential monoamine oxidase inhibitor, was tested on 3 volunteer doctors. Each subject was given a comprehensive list of food and drugs to avoid for a week before the experiment was to start. The pressor amine test was then administered. The subjects took Clorgyline, 5mg morning and midday on the first day, 10mg morning and 5mg midday for 2 days and 10mg morning and midday for 4 days. It was decided that a marked pressor response was to be regarded as a failure in the experimental design. Interaction with oral tyramine and phenylephrine were tested and described. Finally, on the last day, the pressor amine test was repeated. Marked potentiation of the bradycardia induced properties of the amines was found. 9 references. (author abstract modified)

64582
AUTHORS: Barbeau, Andre.
ADDRESS: Department of Neurobiology, University of Montreal, Montreal, Canada
TITLE: L-DOPA therapy: past, present and future.
SOURCE: Arizona Medicine.
SOURCEID: 27(7):1-4, 1970.

Since its introduction in 1961, L-DOPA has become the primary choice for the treatment of Parkinson's disease. By slowly increasing dosages to maximal tolerable levels the general performance has been increased by more than 50 percent in 74 out of 100 patients in 1 study, with similar results in all other samples. The serious side -effects encountered with L-DOPA are postural hypotension, mental changes, and abnormal involuntary movements, and although the dosage apparently controls these side-effects, they must still be considered one of the problems associated with L-DOPA therapy along with the high cost, the 10 percent to 20 percent failure rate, and the metabolism responsible for the low dopamine levels in Parkinson's disease. Future corrections suggested for minimizing side effects of L-DOPA include administration of dopa decarboxylase inhibitors or pancreatic enzymes to increase the amount of drug reaching the brain, or combining other drugs with anti-Parkinson properties with the L-DOPA, or finding analogs of DOPA or dopamine. 24 references.

63596
AUTHORS: Tien, H. C.
ADDRESS: World Journal of Psychosynthesis, Lansing, Michigan
TITLE: Organic integrity test (OIT) in monitoring drug effects.
SOURCE: Psychosomatics.
SOURCEID: 11(5):445-455, 1970.

The organic integrity test (OIT) has proven itself as a useful test in monitoring drug effects. The validity and reliability of the OIT have been independently confirmed by several research workers in the last decade. It was felt, however, that the OIT still needed a different type of confirmation of its validity as a test of organicity, independent of other psychological tests and clinical judgments. The electroencephalogram (EEG) has been chosen for this purpose, and a 1 year EEG - OIT correlation study on 456 adult patients was undertaken. The data, including the age, EEG, abnormality index, OIT score, and clinical diagnosis of each patient were processed in a computer center. The significance tests (t-test) revealed that the OIT is a better test in detecting organic brain dysfunction such as psychosis (e.g. schizophrenia) than the EEG. The overall OIT - EEG correlation (r=-0.39) would indicate that the OIT is a useful test. The effective psychotropic agents (e.g. chlorpromazine, thioridazine, etc.) can reverse the low OIT scores in schizophrenias, involutional psychosis and other organic brain disorders. In therapy, the OIT time - graph is introduced also, and it is shown howthis testing can best be done with daily OIT scores in monitoring drug effects. And the OIT time - graphs can be used profitably to monitor drug therapy, as has been shown in 667 patients on the neuropsychiatric ward of a general hospital, with a variety of diagnoses. In sum, the OIT time - graph is applicable to all neuropsychiatric patients as a daily diagnostic and therapeutic index. 22 references. (Author abstract modified)

63597
AUTHORS: Itil, T.; Keskiner, A.; Heinemann, L.; Han, T.; Gannon, P.; Hsu, W.
ADDRESS: Dept. of Psychiatry, University of Missouri School of Medicine, Missouri Institute of Psychiatry, 5400 Arsenal St., St. Louis, Mo.
TITLE: Treatment of resistant schizophrenics with extreme high dosage fluphenazine hydrochloride.
SOURCE: Psychosomatics.
SOURCEID: 11(5):456-463, 1970.

A group of chronic therapy resistant schizophrenics was treated with extreme high dosage fluphenazine hydrochloride (800mg. daily) and compared with a group of patients who received low dosage of 30mg. daily. Study design was double-blind cross over. Six out of 22 patients showed marked improvement with high dosage, and 3 showed marked improvement with low dosage treatment. Statistical analysis of the global evaluations demonstrated that the high dosage was significantly more effective than the low dosage treatment. More psychotic symptomatology was improved with the low dosage. Extrapyramidal side effects were seen with both dosages, but more frequently with the high dosage. None of the clinical or laboratory side effects continued after the dosage was decreased. The significance of high dosage fluphenazine hydrochloride in the treatment of therapy resistant schizophrenics, from the point of view of therapy and pathogenesis of resistant schizophrenia, has been discussed. 44 references. (Author abstract)

63599
AUTHORS: Goldstein, Burton J.
ADDRESS: Department of Research, University of Miami School of Medicine, Miami, Florida
TITLE: Comparative efficacy of thiothixene capsules and concentrate in acutely schizophrenic patients.

SOURCE: Psychosomatics.
SOURCEID: 11(5):434-437, 1970.

The comparative efficacy of thiothixene capsules and oral concentrate has been tested in acutely schizophrenic patients. The drug has proven to be an effective antipsychotic medication in both forms. The patients in the study were newly admitted to the hospital, over 21 years of age, and selected on the basis of symptoms. Treatment was for 6 weeks. Psychiatric and behavior ratings were obtained on the patients, global evaluation was made, and side effects of the drug forms were noted. The latter were mild to moderate in severity and did not affect the therapeutic value of the drugs. The methods used in the study are discussed. 11 references.

63776

AUTHORS: Simpson, G. M.; Krakov, L.; Mattke, D.; Phard, G. St.
ADDRESS: Early Clinical Drug Evaluation Unit, Rockland State Hospital, Orangeburg, New York
TITLE: A controlled comparison of the treatment of schizophrenic patients when treated according to the neuroleptic threshold or by clinical judgment.
SOURCE: Acta Psychiatrica Scandinavica (Kobenhavn).
SOURCEID: Suppl. 212:38-43, 1970.

A controlled study comparing treatment of 19 chronic schizophrenic patients according to the neuroleptic threshold (Haase's concept) or by clinical judgment is presented. Two groups of patients were randomly selected and treatment with fluphenazine evaluated under double-blind conditions. The 2 treatment procedures were reversed after a substantial interval. There was no difference found between the 2 groups in the therapeutic results. Improvement obtained towards the end of the treatment period suggests that only then were adequate doses being used. 6 references. (author abstract modified)

64286

AUTHORS: Turek, I. S.; Ota, K. Y.; De La Rocha, M.; Agallianos, D.; Kurland, A. A.
ADDRESS: Maryland State Psychiatric Research Center, Baltimore, Maryland
TITLE: The use of molindone in the treatment of acute psychotic states: comparison of two dosage schedules.
SOURCE: Journal of Clinical Pharmacology and the Journal of New Drugs.
SOURCEID: 10(5):349-355, 1970.

The efficacy of molindone HCl (EN-1733-A), a new psychoactive indole derivative, was tested for a period of 6 weeks in 38 newly hospitalized schizophrenic patients using 2 dosage schedules: fixed and escalating. The dosage on both schedules ranged from 10 to 60mg daily. The drug was found to have a moderate neuroleptic effect on nondisturbed psychotic patients. A comparison of 2 dosage schedules, i.e., 5mg b.i.d. initially and fairly uniform dosage increases to a maximum of 60mg versus 10mg t.i.d. initially with subsequent regulation according to patient need, did not reveal differences in therapeutic outcome. The medication was well tolerated. Improvement trends were noted relative to conceptual disorganization, hallucinatory behavior, and tension on both dosage schedules. Other symptoms were not significantly altered. In severely disturbed psychiatric patients, it was necessary to provide other types of sedation. The principal side-effects were postural hypotension and mild extrapyramidal symptoms, which were satisfactorily alleviated through manipulation of dosage and prescription of antiparkinsonian drugs. 9 references. (author abstract)

64331

AUTHORS: Narasimhachari, N.; Heller, B.; Spaide, J.; Haskovec, L.;

Fujimori, M.; Tabushi, K.; Hinwich, H. E.
ADDRESS: Thudichum Psychiatric Research Laboratory, Galesburg State Research Hospital, Galesburg, Illinois 61401
TITLE: Comparative behavioral and biochemical effects of tranylcypromine and cysteine on normal controls and schizophrenic patients.
SOURCE: Life Sciences (Oxford).
SOURCEID: 9(18):1021-1032, 1970.

The behavioral effects evoked by feeding L-cysteine simultaneously with the administration of the monoamino oxidase inhibitor tranylcypromine was studied on a group of 6 controls and 2 chronic schizophrenics. The 8 subjects were placed on a rigorously controlled diet. After a control period of 21 days, all subjects were given 10mg of tranylcypromine 3 times a day for 7 days. On the eighth day L -cysteine was administered in 5g increments up to 20g/day. The combined medications were given for 20 days. The experimentation period was followed by an overload period. In no instance did any of the 6 normal controls exhibit any signs of schizophrenia. Though the normals, like the schizophrenics, revealed increases of urinary tryptamine, unlike the schizophrenics, their chromatograms were negative even for bufotenin, indicating a biological difference between the 2 groups of subjects, namely, that the normals may not be able to dimethylate tryptamines. The close association between the worsening of the schizophrenic symptoms and the increased concentrations and frequency of occurrence in the urine of the 3 N-dimethyl-tryptaminic compounds was noted. An etiological significance of a biochemical factor was indicated by the detection of the urinary N-dimethyltryptamines before behavioral worsening became apparent. 25 references. (author abstract modified)

64431
AUTHORS: Keskiner, Ali; Itil, Turan M.; Todt, Nancy.
ADDRESS: Dept. of Psychiatry, Missouri Institute of Psychiatry, University of Missouri School of Medicine, 5400 Arsenal St., St. Louis, Mo. 63139
TITLE: A comparative study of butaperazine, chlorpromazine and placebo in chronic schizophrenics.
SOURCE: Psychosomatics.
SOURCEID: 11(2):120-126, 1970.

Butaperazine (BPZ), chlorpromazine (CPZ) and a placebo were investigated in 33 chronic schizophrenics. Findings indicate that 1) BPZ is an effective antipsychotic compound in the treatment of chronic schizophrenics, 2) it is more effective than a placebo or CPZ, 3) 1mg of BPZ is more effective than 10mg CPZ and 4) BPZ induces slight to marked degree of extrapyramidal symptoms which can be controlled by antiparkinson medication. 22 references. (author abstract modified)

63598
AUTHORS: Stern, Francis H.
ADDRESS: Department of Medicine, St. Joseph's Hospital, Philadelphia, Pennsylvania
TITLE: Use of a new antidepressant in the female climacteric.
SOURCE: Psychosomatics.
SOURCEID: 11(5):464-466, 1970.

A new antidepressant, pyrovalerone hydrochloride, was tested in an open study on 20 patients in climacteric. The results indicate that a controlled double-blind study of the drug is justified. The symptoms of menopause with which this study was primarily concerned are the mental and emotional alterations; fatigue, depressed moods, boredom, loss of interest, indecision, poor coordination, psychosomatic complaints, anxiety and apprehension. The psychostimulative agent, pyrovalerone hydrochloride, produced improvement in over half of the patients in the symptoms--fatigue, depressed mood and boredom. No patient became worse in these symptoms. Side effects were related to dosage. Nausea and insomnia were the most frequent. 3 references. (Author abstract modified)

63601
AUTHORS: Marshall, Myron H.; Neumann, Charles P.; Robinson, Milton.
ADDRESS: The Silver Hill Foundation, New Canaan, Connecticut
TITLE: Lithium, creativity, and manic-depressive illness: review and prospectus.
SOURCE: Psychosomatics.
SOURCEID: 11(5):406-408, 1970.

A definite relationship links lithium, creativity, and manic-depressive illness. This linkage is examined in the literature and in clinical practice. Review of the literature confirms the linkage but the nature of the linkage requires investigation, and the current studies using lithium in the treatment of manic-depressive patients who are creative in their fields is expected to uncover the actual association. The tie between creativity and psychiatric illness has been discussed for many years. In the present decade, a cult of creativity management has arisen in American industry, and the relationship of creativity and personality has been recognized and considered. Case records are presented to substantiate the thesis that creativity and manic-depressive illness are related. The cases cited in literature and in practice suggest a more than chance association between extreme creativity and the manic swing. It is believed that the effect of lithium ion should reveal evidence that creativity is a substantial result of the mental illness. However, a major problem in the study is the paucity of instruments available for subjective or objective ratings of the creative process. Investigations to date indicate rather strongly that the manic phase inspires a surge of creative output in creative persons with manic-depressive illness. Refinement of a creativity measurement and more intensive study of the patients should further substantiate the thesis. 18 references.

63607
AUTHORS: Caffey, Eugene M., Jr.; Prien, Robert F.
ADDRESS: Psychiatric Division, Neurology and Psychology Service, Department of Medicine and Surgery, Veterans Administration, Washington, D. C.
TITLE: The VA-NIMH study of lithium in affective disorders.
SOURCE: Psychosomatics.
SOURCEID: 11(5):409-412, 1970.

The background, major purposes, the safeguards against potential lithium toxicity, and the informational byproducts of the cooperative clinical study of lithium carbonate administration in affective disorders, jointly supported by the Veterans Administration and the National Institute of Mental Health, are reported. Information is

being collected on syndrome patterns, patient history, family background, and the course of illness following treatment of an acute phase of manic-depressive illness in a 4 year study on the therapeutic and prophylactic efficacy of lithium carbonate in affective disorders. It is hoped that the information will clarify the understanding of manic-depressive illness, the "number 1" major functional psychosis. Patients are selected carefully for this study. There are 3 classifications of patients who are evaluated by 2 clinicians: manic, consisting of patients considered manic-depressive, manic; schizo - affective, consisting of patients considered schizo - affective, manic; and mixed, consisting of patients considered as manic-depressive, manic, by one clinician and schizo - affective, manic, by the other. Evaluation of the patients is described. Once selected, the patients are randomly assigned under modified blind conditions, to treatment with their chlorpromazine or lithium carbonate. A summary of the histories of the patients (approximately 300) admitted to the study, and an account of side effects of prophylactic and therapeutic treatment with lithium and chlorpromazine are recorded. An outpatient study is now underway. Byproducts of the study have been development of an extensive bibliography, and production of a description of the use of lithium carbonate.

64089
AUTHORS: Roxburgh, Peter A.
ADDRESS: Department of Psychiatry, Foothills Hospital, Calgary, Alberta, Canada
TITLE: The present status of lithium therapy in manic depressive psychosis.
SOURCE: Canadian Psychiatric Association Journal (Ottawa).
SOURCEID: 15(2):201-204, 1970.

The significant literature on the use of lithium in manic -depressive psychosis is reviewed. Lithium is highly effective in a proportion of attacks of mania. Its place in the depressive phase in prophylaxis is uncertain. Comments are made on its use in these three areas in the light of its established toxicity. The drug can be tried in cases which are not improved by phenothiazine therapy. Response, if it occurs, is often evident within 48 hr and can be expected within two weeks. Lithium, in its psychiatric usage, is not as dangerous as originally thought. Prodromal toxic effects give sufficient warning and are more sensitive and immediate than routine serum lithium analysis. 16 references. (author abstract modified)

64284
AUTHORS: Baro, Franz; Brugmans, Jo; Dom, Rene; Van Lommel, Renaat.
ADDRESS: Psychiatric Clinic, University of Louvain, Louvain, Belgium
TITLE: Maintenance therapy of chronic psychotic patients with a weekly oral dose of R 16 341. A controlled double-blind study.
SOURCE: Journal of Clinical Pharmacology and the Journal of New Drugs.
SOURCEID: 10(5):330-341, 1970.

A clinical trial of R 16 341 (4,4-chloro-alpha, alpha, alpha-trifluoro-m-tolyl)-1-(4,4-bis(p-fluorophenyl)butyl)-4-piperidinol) was conducted with 38 hospitalized male chronic psychotic patients. In a first stage, 26 patients were treated with a single weekly oral dose of R 16 341 for eight months and 12 patients remained on their baseline maintenance neuroleptic treatment (controls). The 26 patients who had been on R 16 341 then entered a placebo controlled double-blind study for 6 months or until relapse. Therapeutic assessment was made by the Factor Construct Rating Scale (FCRS), Psychiatric Evaluation Questionnaire (PEQ), global rating, graphometric test, and tapping test. In about half the patients, adequate control without side effects was achieved with a weekly oral dose of 10 to 40mg, usually 20mg, of R 16 341. In the other patients, a single weekly oral dose of the antiparkinsonian agent dexbenzetimide, given together with R 16 341, effectively controlled

initial extrapyramidal symptoms (restlessness and akathisia). The FCRS, PEQ, and global rating showed significant improvement (P less than 0.001) in psychotic symptoms during R 16 341 treatment as compared with the previous neuroleptic therapy and the classical treatment received by the control patients. During the double-blind study, the 13 patients on placebo relapsed after 3 to 6 weeks and the 13 patients on R 16 341 maintained the condition achieved in the open study. The graphometric and tapping tests indicated that on the second postmedication day, hypokinesia was more marked than with classical neuroleptic therapy, but coarse motor extrapyramidal symptoms were not more pronounced. On the fourth postmedication day, extrapyramidal impairment was equal or less with R 16 341 as evidenced by the psychiatrists' ratings and the PEQ. Blood analyses revealed no evidence of drug toxicity. 11 references. (author abstract modified)

64317
AUTHORS: Platman, S. R.
ADDRESS: South Beach Psychiatric Center, Brooklyn, New York 11203
TITLE: Comparison of lithium carbonate and imipramine (in prevention of manic-depressive disease).
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(2):132-134, 1970.

A single-blind study was made of 49 patients treated with lithium carbonate and 21 patients treated with imipramine. Lithium carbonate reduced psychotic episodes by 50%, whereas imipramine appeared to have no effect. In those patients receiving lithium carbonate, there was an apparent sex difference, with males showing a more favorable response. In these comparisons the presenting episode was excluded from the data. In comparisons which included the presenting episode, lithium carbonate decreased psychotic episodes by 400% and imipramine showed a 100% improvement. In comparisons of psychotic episodes before and after the test drug, when those occurring within the first 10 weeks of the study were included, neither lithium carbonate nor imipramine had an effect on the course of the illness. 10 references.

64356
AUTHORS: Ota, K. Y.; Turek, I.; Berman, S. A.; Kurland, A. A.
ADDRESS: Spring Grove State Hospital, Maryland Psychiatric Research Center, Catonsville, Maryland
TITLE: A comparative study of fluphenazine-amitriptyline combination and amitriptyline alone in the treatment of depressed psychiatric patients.
SOURCE: Current Therapeutic Research.
SOURCEID: 12(9):585-593, 1970.

The effects of fluphenazine - amitriptyline combination and amitriptyline were compared in a 12 week double-blind study of 106 acutely ill psychiatric patients with depressive symptoms. The patients were treated in a state psychiatric hospital during the first 6 weeks, and in the hospital's outpatient clinic during the second half of the study. The patients received either 2 tablets with 25mg of amitriptyline and 0.5mg of fluphenazine or 25mg of fluphenazine 3 times a day for the first 6 weeks, then 1 tablet 3 times a day for the last 6 weeks. Although both groups significantly improved over the entire treatment course, results indicated the combination to be therapeutically more beneficial for this type of patient in certain psychiatric dimensions. Side effects were minimal, and both medications were found to be well tolerated. Clinical laboratory studies, electrocardiograms, and ophthalmological examinations revealed no significant abnormal findings throughout the 12 week treatment course. 13 references. (author abstract modified)

63595
AUTHORS: Prange, Arthur J. Jr.; Wilson, Ian C.; Lipton, Morris A.; Rabon, A. Mayo; McClae, Thomas K.; Knox, Angelina E.
ADDRESS: University of North Carolina School of Medicine, Chapel Hill, North Carolina
TITLE: Use of a thyroid hormone to accelerate the action of imipramine.
SOURCE: Psychosomatics.
SOURCEID: 11(5):442-444, 1970.

Triiodothyronine (T3), in a dose too small to produce toxicity or factitious hyperthyroidism, can be used to enhance the therapeutic action of imipramine in retarded or nonretarded depressed patients. Whatever the thyroid state of the patient, T3 and imipramine may interact to elevate central adrenergic activity. 13 references. (Author abstract)a

63934
AUTHORS: Kelly, Desmond; Guirguis, Wagih; Frommer, Eva; Mitchell-Heggs, Nita; Sargant, William.
ADDRESS: St. George's Hospital Medical School, London, England
TITLE: Treatment of phobic states with antidepressants: a retrospective study of 246 patients.
SOURCE: British Journal of Psychiatry (London).
SOURCEID: 116(533):387-398, 1970.

A retrospective study of 246 patients presenting with phobicanxiety, who were treated with a monoamine oxidase (MAO) inhibitor, either alone or in combination with chlordiazepoxide or a tricyclic antidepressant, is presented. This treatment, with either a MAO inhibitor alone or in combination with chlordiazepoxide, produced significant improvements in patients who had long-term phobias as their main symptom. There was also a decrease in panic attacks. Patient treatment outcome did not depend upon the depression of the patient, the type of phobia or the personality of the patient. Side-effects included postural hypotension, mydriasis and dry mouth. Restriction of diet was one of the main disadvantages of MAO treatment. Chlordiazepoxide is more effective on free floating anxiety than MAO inhibitors. Children, whose phobias represent a psychological symptom, also do well with MAO inhibitor therapy. 33 references.

64233
AUTHORS: O'Regan, J. B.
ADDRESS: 113 Palisades, Saskatoon, Saskatchewan, Canada
TITLE: Treatment of obsessive-compulsive neurosis with haloperidol.
SOURCE: Canadian Medical Association Journal (Toronto).
SOURCEID: 103(2):167-168, 1970.

A case history of an obsessive-compulsive patient treated with haloperidol as a last resort to frontal lobectomy is discussed. The patient was a 57-year-old retired farmer who could not work or function because of his compulsive behavior and rigid personality. After two hospital admissions in which he received electroconvulsive therapy, which only partially relieved his symptoms, haloperidol (5mg, t.i.d.) was prescribed and his symptoms improved rapidly. Although the subject's depressive mood continued, his compulsive ritualistic behavior almost completely disappeared. It appears as if haloperidol has a specific effect on compulsive behavior. 3 references.

64285
AUTHORS: Kellner, Robert; Claghorn, James L.
ADDRESS: Department of Psychiatry, School of Medicine, University of New Mexico, Albuquerque, New Mexico

TITLE: A controlled trial of Benzoctamine (Ba-30803) in neurotic anxiety.
SOURCE: Journal of Clinical Pharmacology and the Journal of New Drugs.
SOURCEID: 10(5):342-348, 1970.

Seventy neurotic outpatients suffereing from anxiety participated in a trial of benzoctamine. The design was parallel, double-blind, between subjects. Ten patients dropped out from the trial or were excluded for various reasons. The doses compared were benzoctamine, 25mg t.i.d. and 10mg t.i.d., and placebo. Several validated rating and self-rating methods were used. There were no significant differences between the changes in the scores of patients receiving the medication and those receiving placebo. There appeared to be marked individual differences between patients in their responses to the same dose. A few patients were excessively sedated, whereas in others the doses appeared to be inadequate. A fixed dose trial appeared to be inappropriate for the evaluation of the antianxiety effects of this drug. One patient had raised SGOT and SGPT levels which returned to normal after 5 months. A few patients who apparently received doses which were too large for them complained of drowsiness and "feeling drugged." No other significant side-effects were observed. 9 references. (author abstract)

64312
AUTHORS: Houck, John E.
ADDRESS: 1658 Amherst Street, Buffalo, New York 14214
TITLE: Combined therapy in anxiety-depressive syndromes: I. Comparative effects of Limbitrol (chlordiazepoxide-amitriptyline) and placebo.
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(4):269-273, 1970.

Porty neurotic outpatients with moderate or moderately severe depressive reaction associated with anxiety participated in a double-blind placebo-controlled evaluation of the effects of Limbitrol (combination tablet of chlordiazepoxide (5mg) and amitriptyline (12.5 mg). The dosage most often given was 6 tablets per day in three doses and the duration of the study was 6 weeks. Comparison of average improvement scores (difference between predrug and each subsequent rating) at 2, 4, and 6 week evaluation periods showed significant differences for Total Symptomatology (derived from 23 items on the modified Hamilton Depression Scale), Overall Clinical Assessment (physician's) as well as Drug Efficacy Rating (patients'). A trend toward greater improvement on active drug treatment could be discerned for 4 derived symptom clusters, and significant drug placebo differences could be demonstrated for Pathological Thoughts, Somatic Manifestations and Psychomotor Activity, but not for Symptoms of Mood, particularly after 4 to 6 weeks of treatment. The drug combination produced mild but transient drowsiness and dry mouth as well as constipation in a few subjects. 17 references. (author abstract)

64429
AUTHORS: Karkalas, Yani; Lal, Harbans.
ADDRESS: Institute of Mental Health, State of Rhode Island Medical Center, Howard, Rhode Island
TITLE: Imipramine pamoate in hospitalized depressives: a double-blind comparison with placebo.
SOURCE: Psychosomatics.
SOURCEID: 11(2):107-111, 1970.

The use of imipramine pamoate in hospitalized depressives in a double-blind study is described. Imipramine, formulated for oral dosage as the pamoate salt, was compared with a liquid placebo in 40 hospitalized patients suffering from moderate or severe depression. After treatment, systemic evaluation of specific depressive symptoms (Lehmann-Rockcliff scale) showed that mean depressive scores in the drug group decreased significantly when compared to those of the

placebo. The results indicated imipramine pamoate concentrate to be an effective antidepressant in a generally acceptable liquid form. 6 references.

64478
AUTHORS: Stephens, Joseph H.; Shaffer, John W.
ADDRESS: John Hopkins University School of Medicine, Henry Phipps Psychiatric Clinic, 601 N. Broadway, Baltimore, Maryland 21205
TITLE: A controlled study of the effects of diphenylhydantoin on anxiety, irritability, and anger in neurotic outpatients.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(2):169-181, 1970.

In a 6 week double-blind cross over study, diphenylhydantoin, 100mg, t.i.d., was found to be markedly more effective than diphenylhydantoin, 5mg, t.i.d., used as a placebo, in reducing symptoms relating to anger, irritability, impatience, and anxiety in neurotic outpatients. The psychoactive properties of diphenylhydantoin were demonstrated by both self-ratings and physician ratings of change. Improvement when changing from 5mg to 100mg was matched by worsening when changing from 100mg to 5mg. Patients in the controlled study were selected on the basis of the presence of symptoms of anger, irritability, and anxiety, a social class more typical of private patients than clinic patients, and a Barron Ego Strength score of 40 or above. No undesirable side-effects were encountered. 21 references. (author abstract)

64088
AUTHORS: Leung, Albert S. M.
ADDRESS: C. M. Hincks Treatment Center, 440 Jarvis Street, Toronto 284, Canada
TITLE: Lithium carbonate.
SOURCE: Canadian Psychiatric Association Journal (Ottawa).
SOURCEID: 15(2):189-199, 1970.

The pertinent literature on lithium carbonate is reviewed. The drug is examined with respect to its chemistry and source, its absorption, its distribution and retention, its excretion, its biochemistry, and its animal toxicology. Lithium is generally accepted as specifically effective in the treatment of acute manic psychosis and has also been found useful as a prophylactic agent in selected cases of recurrent affective disorders. It has found little use as a antidepressant, and was unsuccessful in treating catatonic excitement, schizo-affective disorders with hyperactivity, epilepsy and behavior disorders. Its potential as a psychotherapeutic adjunct in the management of manic-depressive patients has been reported. Contraindications include cardiovascular and renal diseases, and illnesses associated with electrolyte imbalances. The recommended therapeutic dose is 50mEq/day. Side-effects include gastrointestinal upsets, thirst, tremor, polyuria, electrocardiogram and EEG changes, and nontoxic goiters. Lithium poisoning, its diagnosis, treatment and prevention, is examined. 67 references.

64145
AUTHORS: No author.
ADDRESS: Author address not given
TITLE: Beer sociotherapy can benefit aged mental patients.
SOURCE: Geriatrics
SOURCEID: 25(8):24, 28, 1970.

Beer therapy probably has a high potential for the practical treatment of institutionalized geriatric mental patients. Forty patients (70% with chronic brain syndrome, 30% with functional psychosis) were divided into 4 groups. One group received beer (12oz, once a day) and social therapy (pub-like atmosphere); another was given fruit juice and social therapy; the third group received fruit juice containing thioridazine (20-60mg/day) and sociotherapy; and the fourth group received the drug alone. At the end of 9 weeks, the beer group showed the most improvement in symptoms, cooperativeness, and sociability. The two thioridazine groups also improved, but not as much and the fruit punch group improved the least. Other possible rationales for using this type of therapy include the improvement in a patient's self-esteem resulting from being allowed to drink after a long period of deprivation, the effects of alcohol in reducing social anxiety, and increasing social participation, and the improvement in mentality caused by vasodilation and increased blood supply to the brain.

64188
AUTHORS: Greer, Melvin.
ADDRESS: University of Florida College of Medicine, Gainesville, Florida 32601
TITLE: L-dopa therapy in Parkinson's disease.
SOURCE: Journal of the Florida Medical Association.
SOURCEID: 57(6):23-27, 1970.

An overview of the use of L-dopa in therapy for Parkinson's disease is presented. Briefly discussed are: central nervous system neurohormones, dopamine metabolism in Parkinson's disease and previous drug treatments of Parkinson's disease. L-dopa, a precursor of dopamine, not only offers immediate benefit to the patient but can prevent the progression of the disease. A loading dose of 250mg, 4 times per day, with increments of 0.5gm every 2 or 3 days to a maximum of 8.0gm daily has been used in patients who can tolerate the

speed of dosage increase and the maximum allowable dose. Exceptions are: the aged, the chronically debilitated patient or one whose illness has extended for more than 5 years. Rigidity and bradykinesia have been markedly improved while tremor has not improved as significantly. Side-effects of nausea, vomiting and anorexia have prevented many patients from increasing their total L-dopa intake. Other side-effects include restlessness, aggressiveness, increase in sexual appetite, chewing movements of the tongue, cervical dystonia, and choreiform movements in the extremities. The use of L-dopa in the treatment of Parkinson's disease offers rewards that are of direct clinical benefit but also provide the key for pursuing vital answers to the chemical questions underlying neural function. 30 references.

64610
AUTHORS: Bell, D. S.
ADDRESS: Psychiatric Research Unit, Callan Park Hospital, Rozelle, N.S.W. 2039, Australia
TITLE: The effect of diazepam on the EEG of status epilepticus.
SOURCE: Journal of Neurology, Neurosurgery and Psychiatry (London).
SOURCEID: 32(2):231-237, 1970.

The changes in the EEG of 17 patients during convulsive status treated with intravenous diazepam are reported. The effect of diazepam resembles that of the rapidly acting barbiturates and includes the appearance of burst suppression. The anticonvulsant action of diazepam appears to be unlike the normal inhibitory process of "extinction" that arrests a convulsion. When given during a secondarily generalized convulsion it reversed the spread of the seizure, suggesting that the restriction or impairment of the spread of the discharge is its main anticonvulsant action. The persistence of the seizure discharge after the arrest of the convulsion indicates that the drug probably exerts its principal anticonvulsant or neuronal depressant effect on subcortical structures and that the underlying epileptogenic process may be relatively unaffected by diazepam and continue to follow its own time course. 24 references. (author abstract)

63873
AUTHORS: Denson, R.; Sydiaha, E.
ADDRESS: Psychiatric Services Branch, Saskatchewan Dept. of Public Health, University Hospital, Saskatoon, Saskatchewan, Canada
TITLE: A controlled study of LSD treatment in alcoholism and neurosis.
SOURCE: British Journal of Psychiatry (London).
SOURCEID: 116(533):443-445, 1970.

In order to resolve conflicting reports as to the therapeutic effect of lysergide on alcoholics and neurotics, a test was conducted between two groups, one (25 subjects) receiving up to 5 LSD experiences per subject and one group (26 subjects) receiving standard treatment. The dosage of LSD ranged from 50 to 300 micrograms per treatment. No double or single-blind procedures were employed. Patients were evaluated using the Eysenck Personality Inventory, the IPAT Objective Anxiety Scale, the MMPI, the Lorr Multi-dimensional Rating Scale and the Background and Follow-up Questionnaire for Non-Schizophrenic Patients. No significant differences between the control group and the LSD treated group were observed. 8 references.

64323
AUTHORS: Fischer, Roland; Kappeler, Thomas; Wisecup, Philip; Thatcher, Karen.
ADDRESS: Department of Psychiatry, College of Medicine, Ohio State University, Columbus, Ohio 43210
TITLE: Personality trait dependent performance under psilocybin.
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(2):91-101, 1970.

Measurements of changes in handwriting area and handwriting pressure in 16 volunteers before and after administration of 160 micrograms/kg of psilocybin were used to determine the sensory to motor ratio. This ratio gradually increased on a perception hallucination continuum and was highest during hallucinatory experiences. Except for 2 subjects, there was an increase in the drug induced handwriting area, which was the sensory parameter. For the total sample, the handwriting area increased 25% during the first 110 min after drug administration, whereas the total cumulative handwriting pressure, the motor indicator, increased only 4%. The mean increase for the sensory to motor ratio for the group was 15.9%. Of 4 out of the 16 subjects who decreased their sensory to motor ratios in percent during the first 110 min after administration of the drug, 3 were 'thinkers' and 1 was a 'judger' (in terms of the Myers -Briggs Type Indicator), although the total sample consisted of 7 'thinkers' and 3 'judgers'. The drug induced changes in both handwriting area and average force for the 16 subjects were not interrelated. The drug induced increase in pupillary diameter, which followed a dose response relationship and was a reliable indicator of the level of autonomic arousal, and was unrelated to the drug induced change in the sensory parameter. 30 references.

64388
AUTHORS: Safer, Daniel J.
ADDRESS: Childrens Medical and Surgical Center, 335, Johns Hopkins Hospital, Baltimore, Maryland 21205
TITLE: The effect of LSD on sleep-deprived men.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(5):414-424, 1970.

Thirteen young men were tested to determine the motor, attention, physiologic, and behavioral effects of 1.5mcg/kg of LSD taken orally after 1 or 2 nights' loss of sleep. Twenty additional subjects were tested in 2 control categories: 1.5mcg/kg of LSD alone and 1 night's sleep loss alone. The major significant results of the

study were: The onset of characteristic LSD behavior and attention impairments was more rapid in those men who received LSD after loss of sleep than in the drug alone group; the sleep loss LSD subjects showed inaccuracies in problem solving and vigilance tests not present in the controls; and the men who received LSD after 2 nights' loss of sleep showed increases in pulse rate, pupil size, and 3 hour plasma levels of LSD when compared with those subject groups which received the drug alone and the drug after 1 night's sleep loss. 10 references. (author abstract)

64416
AUTHORS: Jones, Reese T.; Stone, George C.
ADDRESS: Langley Porter Neuropsychiatric Institute, 401 Parnassus Avenue, San Francisco, California 94122
TITLE: Psychological studies of marijuana and alcohol in man.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 18(1):108-117, 1970.

Regular users of marijuana (cannabis sativa) were given smoked and orally administered marijuana, a placebo, or alcohol. They were unable to distinguish between smoked marijuana and the tetrahydrocannabinol free placebo. The oral administration of tincture of cannabis produced primarily dysphoric symptoms and was similar to alcohol in this respect. The smoked marijuana altered pulse rate, time estimation, and EEG, but had no effect on a measure of field dependence or on a digit symbol substitution task. Both drugs appeared to be mild intoxicants in a laboratory setting. Consideration of the dose, prior experience with drugs, setting, and possible cross tolerance of marijuana and alcohol are important in evaluating the significance of the clinical effects. 17 references. (author abstract)

63600
AUTHORS: Dunlop, Edwin.
ADDRESS: Fuller Memorial Sanitarium, Attleboro, Massachusetts
TITLE: Clinical and biochemical aspects of depression.
SOURCE: Psychosomatics.
SOURCEID: 11(5):422-425, 1970.

The clinical and biochemical aspects of depression are examined. Depression as a pathologic symptom of sadness of affect is differentiated from the normal mood by the intensity, duration or quality of the affective state. Depression, as a symptom, may be found in a variety of clinical disorders only some of which are primarily psychiatric. Depression may also refer to 1 or more syndromes or clusterings of symptoms. The term "depression" may also be used to designate 1 or more putative disease entities. Although the notion of the depressions as a group of biologically discrete diseases has considerable historic precedent, and is maintained by many biologically oriented investigators, there are as yet, relatively few biological data upon which to base a meaningful classification of these disorders. The role of serotonin in depression has been very thoroughly investigated. Observations made during the use of drugs for treatment of depression have indicated certain mechanisms of action, as the conjectured action of the antidepressants in altering the metabolism of norepinephrine. Electroshock treatment remains the most reliable treatment for the severe, psychotic depression, but the chemical treatment of depression has reached great importance. Clinical results of treatment with imipramine, amitriptyline and protriptyline hydrochloride are discussed. Effective medication depends upon selection of drug for the particular type of depression, dosage, length of administration, and other factors. It would appear that depressive illnesses are on the increase and certainly occur as a major problem in psychiatry in the world today. This leads to the conclusion that has been established now for some time, that the responsibility for recognition and treatment of depression often goes beyond that of the psychiatrist. It is practical and feasible for any practitioner of medicine to learn the characteristics, signs, symptoms and behavior of depressed patients and with this knowledge and the availability of antidepressant agents, the therapy indicated can be selected with some degree of confidence. (Author abstract modified)

63800
AUTHORS: Balasubramanian, K.; Lucas, S. B.; Mawer, G. E.; Simons, P. J.
ADDRESS: Department of Pharmacology, University of Manchester, Manchester, England
TITLE: The kinetics of amylobarbitone metabolism in healthy men and women.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 39(3):564-572, 1970.

Individual variations in amylobarbitone metabolism were measured in a group of healthy adults to detect any sex dependent differences. Sodium amylobarbitone (3.54mg/kg) was given by intravenous injection to 7 healthy men and 9 healthy women who were not receiving other drugs. Serum amylobarbitone and urine hydroxyamylobarbitone concentrations were measured by gas-liquid chromatography. There was no significant difference between the groups either in the serum amylobarbitone concentration/time curves or in the urinary excretion of hydroxyamylobarbitone. The serum amylobarbitone concentration decayed over 48 hr as a double exponential function of time; the first exponential component had a mean half-time of 0.6 hr (males 0.56 plus or minus 0.06 hr, females 0.62 plus or minus 0.08 hr, plus or minus standard error) and the second exponential component had a mean half time of 21 hr (males 22.7 plus or minus 1.6 hr, females 20.0 plus or minus 1.0 hr, plus or minus standard error). The urinary excretion of hydroxyamylobarbitone over 48 hr accounted for

34% of the dose (males 33.8 plus or minus 3.2%, females 35.2 plus or minus 3.0%, plus or minus standard error). One male and two female subjects excreted hydroxyamylobarbitone partly as a conjugate which was readily hydrolysed in acid. An elimination constant derived from the serum concentration/time curve by the application of a two compartment model was approximately proportional to beta (h(-1 power)), the rate constant of the second exponential component. There was a positive correlation (r equals 0.78, P less than 0.001) between beta and the mean rate of urinary excretion of hydroxyamylobarbitone during the 24 to 48 hr period. 15 references. (author abstract modified)a

63822
AUTHORS: Peaston, M. J. T.; Bianchine, J. R.
ADDRESS: Department of Pharmacology and Therapeutics, Liverpool University, Liverpool 3, England
TITLE: Metabolic studies and clinical observations during L-dopa treatment of Parkinson's disease.
SOURCE: British Medical Journal.
SOURCEID: No. 5693:400-403, 1970.

Metabolic and clinical studies are reported of 14C-L-dopa (L-3,-dihydroxyphenylalanine) administered orally to 22 patients with Parkinson's disease. Residual radioactivity levels in serum, urine, expired air and stool were measured in 9 male patients. Peak serum levels occurred 1 or 2 hours after ingestion, the smallest levels appearing in those patients who had received greater initial doses or who had taken the drug previously. The major pathway of excretion was through the urine with 66% excreted after eight hours; only trace amounts were found in stool or expired air. These results indicate rapid gastrointestinal absorption and subsequent excretion. While improvement was best in younger patients (males) and those patients having had a milder form of the disease for less than 10 years, all of the test group showed an improvement over their prior condition. Improvements from 47% to 60% after treatment from 30 to 100 days, respectively, were noted. Side effects, such as nausea, were experienced during early therapy; choreoathetosis developed in 23% of the patients after continued dosage of 2 months, but the condition was reversed after discontinuing the drug for 48 hours and continuing therapy with a milder dosage. Eighteen percent of the patients experienced hallucinations. Average tolerated dosage was 3g/day with maximum dosage established at 4g/day. 10 references. (author abstract modified)

63874
AUTHORS: Henderson, James G.; Dawson, Audrey A.
ADDRESS: Ross Clinic, Aberdeen, Scotland
TITLE: Serum vitamin-B12 levels in psychiatric patients on long-term psychotropic drug therapy.
SOURCE: British Journal of Psychiatry (London).
SOURCEID: 116(533):439-442, 1970.

Forty six psychiatric patients (27 male and 19 female), who had been receiving psychotropic drugs for many years, were studied to determine the possible effects of these drugs on serum levels of vitamin B12. The research group was compared with a control group of 96 (60 male and 36 female) who were matched with respect to age, sex, and psychiatric diagnosis. None of the study group had serum vitamin B12 levels low enough to warrant further investigation. In another study, each of the commonly used psychotropic drugs was added to serum having a known level of vitamin B12. At concentrations of 10 micrograms per ml serum of the drug, no change was observed in B12 levels. 8 references.

63927
AUTHORS: Parker, Kenneth D.; Crim, M.; Elliott, Henry W.; Wright, James A.; Nomof, Norman; Hine, Charles H.
ADDRESS: Author address not given

TITLE: Blood and urine concentrations of subjects receiving barbiturates, meprobamate, glutethimide, or diphenylhydantoin.
SOURCE: Clinical Toxicology.
SOURCEID: 3(1):131-145, 1970.

The blood concentrations of sedative - hypnotics following doses which may impair judgment, coordination, and skill but not produce unconsciousness were studied. Adult volunteer male prisoners were given oral doses of pentobarbital (600mg), secobarbital (600mg), amobarbital (600mg), butabarbital (600mg), phenobarbital (600mg), meprobamate (1600mg), glutethimide (2000mg), and diphenylhydantoin (600mg). Onset and degree of CNS depression were estimated and correlated with drug concentrations in blood. Excretion of unchanged drugs was followed for 21 hr by analysis of urine and urine/blood drug concentration ratios were calculated. Blood concentrations of the barbiturates used in this study were compared with values from the literature for victims of barbiturate poisoning. 34 references. (author abstract modified)

63939
AUTHORS: Flach, Frederic F.; Faragalla, Farouk F.
ADDRESS: Department of Psychiatry, New York Hospital, New York, New York 10021
TITLE: The effects of imipramine and electric convulsive therapy on the excretion of various minerals in depressed patients.
SOURCE: British Journal of Psychiatry (London).
SOURCEID: 116(533):437-438, 1970.

Fourteen depressed patients were used to explore the relationship between electric convulsive therapy (ECT) or imipramine therapy (150mg/day) and increased urinary calcium levels and changes in the excretion of other metabolites such as phosphate, magnesium, sodium and potassium. ECT and imipramine therapy were associated with shifts in electrolyte excretion which varied among the patients studied. The common denominator in these shifts was the observable decrease in urinary calcium which was preceded or accompanied by a change of the measured electrolytes. Metabolic shifts in mineral metabolism associated with ECT or imipramine, may have beneficial effects in the process of recovering from depression. 3 references.

64097
AUTHORS: Chase, T. N.; Schnur, J. A.; Gordon, Edna K.
ADDRESS: Laboratory of Clinical Science, National Institute of Mental Health and Epidemiology Branch, Bethesda, Maryland 20014
TITLE: Cerebrospinal fluid monoamine catabolites in drug-induced extrapyramidal disorders.
SOURCE: Neuropharmacology (Oxford).
SOURCEID: 9(3):265-268, 1970.

The effects of antipsychotic drugs on CSF monoamine catabolite levels was studied. Levels of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in lumbar CSF were measured in 20 female psychiatric patients. Those receiving long-term treatment with antipsychotic drugs who remained free of extrapyramidal dysfunction had substantially higher concentrations of these monoamine catabolites than patients not taking these drugs. Individuals who developed parkinsonian or dyskinetic signs while receiving antipsychotic agents appeared to have significantly lower concentrations of both HVA and 5-HIAA than patients not manifesting these disorders despite similar drug exposure. The foregoing observations support the hypothesis that the compensatory acceleration of cerebral monoamine metabolism induced by antipsychotic drugs may be impaired in patients who develop extrapyramidal dysfunction. 22 references. (author abstract modified)

64387
AUTHORS: Safer, Daniel J.
ADDRESS: Childrens Medical and Surgical Center, 335, Johns Hopkins Hospital, Baltimore, Maryland 21205
TITLE: The concomitant effects of mild sleep loss and an anticholinergic drug.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(5):425-433, 1970.

Thirty seven young men were tested in drug alone, sleep loss alone, and sleep loss drug groups to determine the separate and combined effects of mild sleep loss and scopolamine hydrobromide. Scopolamine was administered intravenously in either a sedative dose (5mcg/kg) or a low deliriant dose (10mcg/kg); sleep deprivation was for either 1 or 2 nights. Attention, accuracy, motor skill and behavior were measured and rated. An analysis of the results revealed that either dose of scopolamine given after loss of sleep caused significantly more intense and prolonged psychotomimetic effects than were noted in the drug alone condition. Unlike the psychotomimetic effects, the results on sedation were not uniform. Those men who received 5mcg/kg of scopolamine following sleep deprivation showed increased somnolence, whereas the reverse was true for the 10mcg/kg scopolamine-sleep-loss subjects. 12 references. (author abstract)

64474
AUTHORS: Kornetsky, Conan.
ADDRESS: Division of Psychiatry, Boston University School of Medicine, Boston, Massachusetts 02118
TITLE: Psychoactive drugs in the immature organism.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(2):105-136, 1970.

A number of avenues of approach to the study of the effects of drugs on children are presented. Many investigators have begun to classify the behavior of disturbed children on a number of sophisticated, but operationally simple procedures which allow some dissection of the behavior deficits. An understanding of the manner in which amphetamines produce their therapeutic effect on the hyperkinetic child cannot be forthcoming from studies that only elaborate the pathological behavior. More attention must be paid to the function of the central and autonomic nervous systems and how these systems relate to the behavior of the child. Attention should be directed toward animal models for understanding some of the behavior disorders. Studies could be directed toward giving us a more complete grasp of the aberrant behavior seen in the human child. Animal models can complement studies in humans and they have the further advantage of allowing a more complete biochemical and neuropharmacological study of behavior. 83 references. (author abstract modified)

64524
AUTHORS: No author.
ADDRESS: Author address not given
TITLE: Parkinsonism.
SOURCE: Medical Journal of Australia (Sydney).
SOURCEID: 1(15):742-743, 1970.

Central nervous system synaptic chemotransmission substances presently include noradrenaline, dopamine, 5-hydroxytryptamine, acetylcholine and gamma-aminobutyric acid; the basal ganglia appear to sponsor cholinergic (excitatory function) and dopaminergic (inhibitory) transmission at synaptic junctions. The concept of cholinergic dominance in symptoms of parkinsonism appears established from a variety of evidential paths, and constitutes a rational basis for use of drugs with anticholinergic action in treatment of parkinsonism (benzhexol, procyclidine and biperiden, with other atropine-like compounds, and antihistamine drugs such as ethopropazine and orphenadrine); however, it also follows that

symptoms of parkinsonism will be relieved if cholinergic dominance is reduced by increased dopaminergic activity. Dopamine p.o. does not enter neural parenchyma, but its immediate precursor, L-dopa (dihydroxyphenyalanine), in gradually increasing dosage, produces substantial improvement in 50-75% of patients. Amantadine hydrochloride (an antiviral agent) has been shown to improve 66% of 163 parkinsonism patients. These chemotherapeutic results should not overshadow the benefits of stereotactic surgery, which achieves a 30 to 50%improvement, and is of particular value in relieving akinesia and rigidity. 10 references.

63774
AUTHORS: Simpson, G. M.; Krakov, L., Kunz-Bartholini, Esther.
ADDRESS: Early Clinical Drug Evaluation Unit, Rockland State Hospital, Orangeburg, New York
TITLE: A controlled trial of combined medications on behavioral and extrapyramidal effects.
SOURCE: Acta Psychiatrica Scandinavica (Kobenhavn).
SOURCEID: Suppl. 212:20-27, 1970.

A controlled trial is reported of combined medications on behavioral and extrapyramidal effects in 24 chronic schizophrenic patients. Under double-blind conditions, the effects of increasing amounts of perphenazine, or a perphenazine - amitriptyline combination were administered to 2 groups of patients, who were already receiving "optimal" therapeutic dosages of perphenazine. Both groups exhibited slight behavioral improvement and significantly diminished extrapyramidal side effects were noted in the group receiving the combination of drugs. Any order effect was eliminated by a double-blind crossover study. Therapeutic implications of these findings are briefly discussed. The use of this combination of medications results in more behavioral improvement from a greater tolerance of perphenazine, plus the additive effect of amitriptyline. 22 references. (author abstract modified)

63775
AUTHORS: Angus, J. W. S.; Simpson, G. M.
ADDRESS: Early Clinical Drug Evaluation Unit, Rockland State Hospital, Orangeburg, New York
TITLE: Handwriting changes and response to drugs -- a controlled study.
SOURCE: Acta Psychiatrica Scandinavica (Kobenhavn).
SOURCEID: Suppl. 212:28-37, 1970.

The relationship between the therapeutic response to a neuroleptic drug and the handwriting changes which it produces is described. In a controlled study of 2 matched groups of 9 schizophrenics, the clinical state of the patient was related to dosage of thiothixene above and below the neuroleptic threshold. The mental state of the patients was rated each week by 2 research psychiatrists. Results support an earlier view by Haase that once the handwriting changes have occurred, the patient is receiving optimal medication. 11 references.

63777
AUTHORS: Simpson, G. M.
ADDRESS: Early Clinical Drug Evaluation Unit, Rockland State Hospital, Orangeburg, New York
TITLE: Controlled studies of antiparkinsonism agents in the treatment of drug-induced extrapyramidal symptoms.
SOURCE: Acta Psychiatrica Scandinavica (Kobenhavn).
SOURCEID: Suppl. 212:44-51, 1970.

Four experiments designed to assess the effect of antiparkinsonism drugs on phenothiazine produced parkinsonism are described. Twelve male patients with drug induced extrapyramidal symptoms were rated with manual dexterity and psychomotor tests, a neurological rating scale and changes in handwriting. When intravenous injections of benztrapine mesulate and biperiden were employed, it was difficult to distinguish the effects of the active drug from the placebo. When handwriting was used as an indication, it was possible to distinguish the oral administration of benztropine mesylate from a placebo. The trials of intravenous preparations in the treatment of parkinsonism are seen to be invalid. 10 references. (author abstract modified)

63879 [redacted]
AUTHORS: Goldstein, Leonide; Graedon, Joseph; Willard, David; Goldstein, Francis; Smith, Robert E.
ADDRESS: Neuropharmacology Section, New Jersey Neuropsychiatric Institute, Princeton, New Jersey
TITLE: A comparative study of the effects of methaqualone and glutethimide on sleep in male chronic insomniacs.
SOURCE: Journal of Clinical Pharmacology and the Journal of New Drugs.
SOURCEID: 10(4):258-268, 1970.

The effects of 2 nonbarbiturate sleep inducing compounds were tested on a group of chronic insomniacs. It was felt data obtained under such conditions would be more representative of the therapeutic situation than if the drug were tested on normal sleepers. Methaqualone (300mg) and glutethimide (500mg) were administered during 3 consecutive nights to 10 chronic insomniac subjects. This was preceded by 3 nights of placebo control recordings and followed by 4 nights of placebo recovery recordings. Methaqualone reduced wakefulness, increased stage 3, and decreased stage 4 sleep. It did not affect REM sleep. Glutethimide decreased stage 3 and REM sleep. Following withdrawal, there was, with methaqualone, a carryover of the reduction of wakefulness and of the decrease of stage 4 sleep. A surprising increase in REM sleep was found. Following glutethimide, there was no carryover of the decrease in wakefulness. REM time was increased. 24 references. (author abstract modified)

63978
AUTHORS: Firth, H.; Lewis, S. A.; Ogunremi, O. O.; Oswald, I.
ADDRESS: Department of Psychiatry, Royal Edinburgh Hospital, Morningside, Edinburgh, EH10 5HF, Scotland
TITLE: The effect of acute administration of (meta trifluoromethyl-phenyl)-1-(benzoyl oxy) ethyl amino-2-propane (780 SE) and fenfluramine on human sleep.
SOURCE: British Journal of Pharmacology (London).
SOURCEID: 39(2):462-463, 1970.

The effect of 300 mg of (meta trifluoro methyl-phenyl)-1-(benzoyl oxy)ethyl amino-2-propane (780 SE) and 40 mg of fenfluramine on nocturnal sleep patterns in male subjects is related. Electrodes were attached in standard eye locations for recording of eye movements and to the scalp for EEG recording. The drugs or placebo were administered 30 minutes before retirement. 780 SE was found to increase the amount of stage I sleep and the number of shifts to stages I (drowsiness) or W (arousal). Increased amount of stage I was associated with decreased percentages of stages 3 and 4 (19.1%) when compared with placebo results (28.5%). Fenfluramine also was found to increase time spent in stage I without other significant changes. These two compounds thus have no effect on the REM phase of sleep in contrast to other amphetamines, although they did disturb sleep by increasing the number of shifts to stages I and W. 9 references.

64074
AUTHORS: Tobin, J. M.; Brousseau, E. R.; Lorenz, A. A.
ADDRESS: Northwest Psychiatric Clinic Research Center, Eau Claire, Wisconsin
TITLE: Clinical evaluation of haloperidol in geriatric patients.
SOURCE: Geriatrics.
SOURCEID: 25(6):119-122, 1970.

Haloperidol was evaluated in 18 geriatric patients to determine its effectiveness in the control of psychomotor agitation and certain other symptoms accompanying organic brain impairment associated with aging. This patient population improved under treatment with haloperidol. The improvement consisted of increased patient manageability and reduced severity of various undesirable symptoms. Psychomotor agitation, the principal target symptom in this group, showed an impressive reduction. Other symptoms reduced appreciably were hallucinations, disorientation, withdrawal, anxiety, depression,

confusion, and delusions. There was no evidence of any systemic toxic effects resulting from haloperidol, and side-effects were rare. The lack of hypotensive effects in these patients suggests that haloperidol may be preferable to the phenothiazines in the treatment of mental disorders of the aged. 11 references. (author abstract)

64113
AUTHORS: Rechtschaffen, J. S.
ADDRESS: Beekman-Downtown Hospital, New York, New York
TITLE: Treatment of depression by the internist: results with imipramine.
SOURCE: Clinical Medicine.
SOURCEID: 77(6):18-22, 1970.

The effects of imipramine on (1) specific depressive symptoms and (2) overall response in depressed patients treated in a general practitioner's or internist's office were studied. Under the careful supervision of a physician specializing in internal medicine, 51 patients with reactive depression (37), postmenopausal depression (11), or senile depression (3) received imipramine, usually 75mg daily for 2 to 4 months. Nearly all had chronic physical illnesses. At the end of the treatment period, 74 percent of the patients had obtained complete or partial improvement of depressive symptoms. Imipramine was generally well tolerated. Minor side effects developed in 9 patients, 4 of whom discontinued therapy. It was concluded that imipramine is a safe and effective antidepressant for use in a nonpsychiatric setting. 13 references. (author abstract modified)

64152
AUTHORS: Sourander, L.; Ruikka, I.; Rautakorpi, J.
ADDRESS: City Hospital, Turku, Finland
TITLE: Psychological methods applied to evaluate symptomatic geriatric treatment.
SOURCE: Geriatrics.
SOURCEID: 25(8):124-125, 128, 132, 136-137, 1970.

The effects of psychosedatives, neuroleptics and vasodilator drugs in the treatment of psychic disorders in geriatric, nonpsychotic patients is studied. Two groups of subjects (receiving placebo or combination of 0.05gm dixyrazine and 1.2gm inositol nicotinate twice a day) were evaluated by psychometric measures which included reaction time, sense of balance and perception of vertical and horizontal with body tilt. The reaction time decreased in men receiving combination treatment at a weak significance level, whereas the reaction time wrong reactions decreased in both sexes at the 99% significance level. The performance of the drug treated men was significantly better in the test for sense of balance in 2 of the 3 test variables and of the women in one of the variables. In the test for perception of vertical and horizontal with body tilt, the performance was better in men in 4 of 8 variables; however, in women, no significant differences were noted. A combination of dixyrazine and inositol nicotinate apparently has an improving effect on sensorimotor abilities of aged, long-stay hospital patients. 6 references.

64386
AUTHORS: Johnson, G.; Friedhoff, A. J.; Alpert, M.; Marchitello, J.
ADDRESS: Medical Research Division, Schering Corporation, Bloomfield, New Jersey 07003
TITLE: Effects of N-acetyl dimethoxyphenethylamine (NADMPEA) in man.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(5):434-438, 1970.

The effects of N-acetyldimethoxyphenethylamine in human volunteers was evaluated in a modified rising dose tolerance test. (This compound is more potent in rats than the parent compound, 3,4-

dimethoxyphenethylamine, and its behavioral profile in rats suggested a possible hallucinogenic action in man.) Patients with acute schizophrenia and normal volunteers were tested. Doses ranged from 1.3 to 16.4mg/kg without any hallucinogenic effect. A pharmacological effect and drug induced tremor was seen at higher doses. 9 references. (author abstract)

64389
AUTHORS: Idestrom, C.-M.; Schalling, D.
ADDRESS: Department of Experimental Psychiatry, Karolinska Institutet, S-104 01 Stockholm 60, Sweden
TITLE: Objective effects of dexamphetamine and amobarbital and their relations to psychasthenic personality traits.
SOURCE: Psychopharmacologia (Berlin).
SOURCEID: 17(5):399-413, 1970.

Objective effects of 5 and 15mg dexamphetamine and 150 and 300mg amobarbital were studied in 2 groups of 22 military subjects, selected on the basis of extreme scores on a psychasthenia scale. Blood pressure, pulse rate and performance on psychomotor, perceptual and cognitive tests were measured before, 1 hour and 2 hours after intake of capsules containing a drug dose or placebo. The drug conditions were rotated and the procedure was double-blind. The general pattern of drug effects was as expected; improvement after dexamphetamine and impairment after amobarbital, when compared to placebo. This pattern was illustrated as reflecting an activation continuum, the lowest activation being noted on 300mg amobarbital and the highest on 15mg dexamphetamine. Dexamphetamine gave few significant effects except for the cardiovascular measures. Significant effects were obtained after amobarbital in a number of tests. The treatment group interactions noted appeared to be related to a greater sensitivity to amobarbital in the high psychasthenia group. More significant effects were obtained after amobarbital as compared to placebo in this group than in the low psychasthenia group, especially 1 hour after 300mg amobarbital. 26 references. (author abstract)

63753
AUTHORS: Clement, W. R.; Solursh, L. P.; van Ast, Walter.
ADDRESS: Department of Psychology, Queen Street Mental Health Center, 999 Queen Street W., Toronto 145, Ontario, Canada
TITLE: Abuse of amphetamine and amphetamine-like drugs.
SOURCE: Psychological Reports.
SOURCEID: 26(2):343-354, 1970.

The present use of amphetamine type compounds in Toronto, Canada is examined carefully. Their pharmacology, side-effects and rationale in low dose use are described. The history, syndrome and complications of high dose amphetamine abuse are also presented. A survey was taken of the preparedness of the medical profession of Toronto to treat the problems presented by chronic use of amphetamine compounds. Treatment in several large hospitals was found inadequate. Attempts to obtain laboratory examination of physiological factors related to amphetamine use met with almost no success. Thus, Toronto was not well prepared to cope effectively with the increasing abuse of amphetamines and similar compounds. Several recommendations given to combat amphetamine abuse were: 1) discontinuation of the drug with brief hospitalization and close supervision; 2) use of ammonium chloride and a minor tranquilizer; 3) use of an anticonvulsant when necessary; 4) use of an anti-agitational compound with supportive psychotherapy, and 5) social assessment and manipulation. 47 references.

63778
AUTHORS: Angus, J. W. S.; Simpson, G. M.
ADDRESS: Early Clinical Drug Evaluation Unit, Rockland State Hospital, Orangeburg, New York
TITLE: Hysteria and drug-induced dystonia.
SOURCE: Acta Psychiatrica Scandinavica (Kobenhavn).
SOURCEID: Suppl. 212:52-58, 1970.

Case material is reviewed relating the concept of hysteria to drug induced dystonia. The dystonic reactions produced by phenothiazinesand complex phenomena corresponding to them may lead to mistaken diagnosis of catatonia, catalepsy, akinetic mutism, euphoria, depression, oculogyric crisis, conversion reaction, epilepsy, narcolepsy, dyskinesis, encephalitis or tetanus. The relationshipof these phenomena to those of hysteria is discussed. Abolishing artificial distinctions between the "organic" and the "functional" approaches to disease is suggested. The interdependence of psychological and neurophysiological events must be the basis for research. 29 references.

63845
AUTHORS: Van Woert, Melvin H.
ADDRESS: Department of Internal Medicine, Division of Clinical Pharmacology, Yale University School of Medicine, New Haven, Connecticut
TITLE: Pharmacodynamics of 3,4-dihydroxyphenylalanine (DOPA) in Parkinson's disease.
SOURCE: Connecticut Medicine.
SOURCEID: 34(6):401-405, 1970.

The side effects as well as the therapeutic efficacy of L-dopa in the treatment of Parkinsonism are demonstrated in 34 patients treated at Yale - New Haven Hospital. With daily doses ranging from 2 to 7.5gm depending on individual tolerance, bradykinesia, rigidity, and gait were improved to a greater degree (better than 50% improvement in 23, 21, and 20 patients respectively for each symptom) than tremor (better than 50% improvement in only 11 patients). Seborrhea, sialorrhea, speech, handwriting, facial expression, and posture were also considerably improved while dysarthria and muscle weakness did not respond to L-dopa. Common side-effects among the patients include anorexia (16 patients), nausea and vomiting (18

patients), dyskinesias (12 patients), postural hypotension (9 patients), lightheadedness (8 patients), and insomnia (8 patients). Biochemical changes which occur with L-dopa administration are elevated blood urea nitrogen, serum glutamic oxaloacetic transaminase, uric acid, leukopenia, and a positive direct Coombs test. 25 references.

63854
AUTHORS: Ettinger, Milton; Curran, John.
ADDRESS: Department of Neurology, Hennepin County General Hospital, Minneapolis, Minnesota
TITLE: Liver disease and phenothiazines; involuntary movements.
SOURCE: Minnesota Medicine.
SOURCEID: 53(7):731-736, 1970.

The possibility of misdiagnosis of an acquired hepatocerebral degeneration as the clinically similar tardive dyskinesia syndrome, a side-effect of phenothiazine administration, was determined by examining 8 patients at the Fergus Falls State Hospital who had been identified 3 years earlier as possible cases of the syndrome. Based on a normal bromsulphalein retention after 30 minutes of less than 10%, 3 and possibly 4 of the patients (57%) probably had liver disease, and 1 was diagnosed as hepatocerebral degeneration. Nocase of tardive dyskinesia syndrome can be considered definitely as such, unless adequate hepatic function tests have been performed. 12 references.

63880
AUTHORS: Neu, Richard L.; Powers, Harold O.; King, Saddie; Gardner, Lytt I.
ADDRESS: Department of Pediatrics, State University of New York, Upstate Medical Center, Syracuse, New York
TITLE: Delta8- and delta9-tetrahydrocannabinol: effects on cultured human leucocytes.
SOURCE: Journal of Clinical Pharmacology and the Journal of New Drugs.
SOURCEID: 10(4):228-230, 1970.

The effect of delta8-tetrahydrocannabinol (D8-THC) on chromosomes in human blood cultures was studied. D8-THC was added to human leucocyte cultures to give final concentrations of 30, 35, 40 and 45mcg/ml of medium. A decrease in the mitotic index with increasing concentrations of D8-THC was noted, but no structural rearrangements were observed. D8-THC did not increase the number of breaks and/or gaps over those found in control cultures (less than 5%). In preliminary experiments D9-THC has shown similar findings. 9 references. (author abstract modified)

63897
AUTHORS: Pivers, M.; Horner, Bennett.
ADDRESS: 140 Wallace Street, Nanaimo, British Columbia, Canada
TITLE: Possible lethal reaction between Nardil and dextromethorphan.
SOURCE: Canadian Medical Association Journal (Toronto).
SOURCEID: 103(1):85, 1970.

The case history of a woman (26 years of age), treated for depression with Nardil, 15mg 4 times daily, is reported. She consumed approximately 2 ounces of a cough preparation containing dextromethorphan 6 hours following a double dose of Nardil. Nausea, dizziness and collapse ensued 30 minutes after ingestion of the cough mixture, and on admittance to hospital she was severely hypotensive (systolic pressure below 70mm Hg), unconscious with rigid extremities and fixed dilated pupils, and with a temperature of 42 to 42.2 degrees centigrade. Death ensued 4.25 hours after admission due to cardiac arrest. Autopsy findings revealed dextromethorphan in the stomach content but no evidence of Nardil, barbiturates, tranquilizers, sedatives or alcohol. The probable cause of death was

a toxic reaction resulting from the combination of Nardil and dextromethorphan.

64168
AUTHORS: Maher, John F.
ADDRESS: University of Missouri, Medical Center, 807 Stadium Blvd., Columbia, Missouri 65201
TITLE: Determinants of serum half-life of glutethimide in intoxicated patients.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 174(3):450-455, 1970.

To determine factors that influence the disappearance of glutethimide from serum of intoxicated patients an evaluation was made by determination of the levels in serum sampled before and after various types of therapy. The calculated duration of time for a serum level to be reduced to half its initial value, the serum half-life in intoxicated patients, averaged 40.1 hours. The half-life in patients treated with hemodialysis was 14.6 hours. Renal failure did not prolong the serum half-life nor did diuresis shorten it. There was a positive correlation between the serum level and the serum half-life, r equal to 0.56. This is interpreted as consistent with rate limited enzymatic degradation of glutethimide. The serum half-life did not correlate with the time interval after ingestion in this group of patients. In some patients with hypotension the serum half-life was prolonged, suggesting impaired perfusion of tissue responsible for elimination of glutethimide, presumably the liver. 5 references. (author abstract)

64236
AUTHORS: Ginsberg, Myron D.; Hertzman, Marc; Schmidt-Nowara, Wolfgang W.
ADDRESS: Harvard Medical Unit, Boston City Hospital, Boston, Massachusetts
TITLE: Amphetamine intoxication with coagulopathy, hyperthermia, and reversible renal failure: a syndrome resembling heatstroke.
SOURCE: Annals of Internal Medicine.
SOURCEID: 73(1):81-85, 1970.

A case report is given of a patient who ingested 2g of amphetamine. The subject was admitted with symptoms of delirium, hyperkinesia, hyperthermia, rapid pulse, hypertension, dilated pupils and blanched skin. Chlorpromazine (100mg, i.m.) and pentobarbital (i.v.) were administered, ice water immersion was undertaken to reduce body temperature and the bladder was catheterized to monitor renal function. Although the temperature and cardiovascular abnormalities rapidly returned to normal limits, the patient subsequently developed renal failure and intramuscular hemorrhaging. Albuminuria, azotemia and isothenuria were noted in association with these events. Careful management of multiple physiological systems in the patient suffering from amphetamine abuse is therefore necessary in the treatment of the intoxication. 22 references.

64268
AUTHORS: Gogan, M. P.; Ritson, E. B.
ADDRESS: Sheffield Regional Addiction Service, Sheffield, England
TITLE: Dimyril abuse in the East Midlands.
SOURCE: British Journal of Addiction (London).
SOURCEID: 65(1):63-66, 1970.

The importance of availability of drugs in the problem of abuse is demonstrated in 6 patients admitted to the Sheffield Region Addiction Unit who abused Dimyril (a nonprescription cough suppressant). All the patients claimed that they experienced euphoria 1 to 1.5 hours after taking 20 to 200cc p.o. Dimyril and 4 claimed that they felt relaxed. Urine samples tested regularly negated the possibility that amphetamines, opiates, or other commonly abused

drugs had been taken. Commonly occurring side-effects with Dinyril included visual hallucinations, abdominal pains, and insomnia nightmares, while anxiety, time distortion, delusions, muscle stiffness, and glitter phenomena were also reported.

64287
AUTHORS: Downing, R. W.; Rickels, K.; Meyers, F.
ADDRESS: Department of Psychiatry, University of Pennsylvania, Philadelphia, Pennsylvania
TITLE: Side reactions in neurotics: I. A comparison of two methods of assessment.
SOURCE: Journal of Clinical Pharmacology and the Journal of New Drugs.
SOURCEID: 10(5):289-297, 1970.

Two methods of collecting information about side reactions were compared in 123 neurotic patients drawn from both clinic and private practice settings and treated over a 4 week period with antidepressants, tranquilizers or placebo. During their final treatment interview, patients were asked, "How did the medication make you feel?", and their responses were noted on a Side Reaction Recording Sheet. This procedure was designated as the open ended method. Subsequent to this, patients were given a 28 item Side Reaction Questionnaire. They were asked to rate the intensity and discomfort of each of the symptoms which applied to them and to state whether they felt each was due to their medication. This procedure was designated as the structured method. The incidence of side-effects (the number of patients with one or more side-effects), and the number of side effects per patient were found to be significantly higher with the structured method for antidepressant and tranquilizer but not for placebo patients. The 2 methods agreed in the identification of 69% of the patients as either side reactors or nonside reactors. Patients identifying themselves as side reactors by the open ended but not by the structured method were considered to be reporting unreliably. They constituted 7.3% of the total sample. Evidence was presented that drug treated patients reporting one or more side reactions with the structured method but no side reactions with the open-ended method were doing so because explicit questioning was calling their attention to mild, drug induced symptomatology which they had previously overlooked or failed to relate to their medication. This method did not simply suggest side-effects. Finally, it was shown that of the 2 methods, the structured method is more likely to lead to the conclusion that the incidence of side-effect resulting from a given drug is higher than that resulting from placebo. 9 references. (author abstract modified)

64316
AUTHORS: Shopsin, Baron.
ADDRESS: Neuropharmacology Research Unit, New York University School of Medicine, 550 First Avenue, New York, New York 10016
TITLE: Effects of lithium on thyroid function (a review).
SOURCE: Diseases of the Nervous System.
SOURCEID: 31(4):237-244, 1970.

The effects of lithium ion on the thyroid and its possible role in bringing about endocrine disturbances are reviewed together with thyroid disturbance and its relation to manic-depressive illness and the effects of psychoactive drugs on thyroid function. No consistently predictable effects on thyroid function could be attributed to lithium and other psychotropic drugs (perphenazine, chlorpromazine). Lithium does interfere with the production of thyroxin and does result in goiter; both conditions are readily reversed when lithium is discontinued or when thyroid hormone is administered concurrently with this medication. A relationship between the thyroid gland and mental illness has long been suspected, although the role played by the thyroid in this regard remains obscure. Infants born with thyroid hormone deficiency show mental

retardation of varying severity. There are scattered reports of schizophrenia being treated successfully with thyroid hormone, although other studies have shown that a persistent abundance of thyroid hormone can lead to full blown psychosis. 56 references.

64420
AUTHORS: Prindle, Kirk H., Jr.; Gold, Herman K.; Cardon, Philippe V.; Epstein, Stephen E.
ADDRESS: Cardiology Branch, National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland 20014
TITLE: Effects of psychopharmacologic agents on myocardial contractility.
SOURCE: Journal of Pharmacology and Experimental Therapeutics.
SOURCEID: 173(1):133-137, 1970.

The effects of lithium chloride, chlorpromazine (Thorazine), diazepam (Valium) and chlordiazepoxide (Librium) on the intrinsic contractile properties of isolated cat papillary muscles were studied in order to gain more knowledge concerning their use with cardiac patients as regards myocardial contractility. Lithium chloride at a concentration of 4.0mEq/liter significantly increased peak isometric tension and the rate of tension development. Tension at 10mEq/liter increased by an average of 21% from the control. At this concentration, the rate of tension development increased 33% from the control. Chlorpromazine and chlordiazepoxide produced no changes at concentrations that encompassed the range of blood levels found in patients being treated with these drugs. At higher concentrations, decreases in tension and rate of tension development were observed. The addition of diazepam over a wide range of concentrations failed to produce any significant changes in papillary muscle contractility. 22 references. (author abstract modified)t

64622
AUTHORS: Robinson, Donald S.; Sylwester, David.
ADDRESS: University of Vermont College of Medicine, Burlington, Vermont 05401
TITLE: Interaction of commonly prescribed drugs and warfarin.
SOURCE: Annals of Internal Medicine.
SOURCEID: 72(6):853-856, 1970.

The recognition of drugs that interact with warfarin has clinical relevance because of potential serious reactions as a result of the complexities of multiple drug therapy. Because of their frequent use in patients requiring anticoagulant therapy, 4 drugs -- chlordiazepoxide, secobarbital, amobarbital, and chlorothiazide -- were studied in 8 subjects for possible interaction with warfarin. Daily dosages during the study were chlorothiazide, 1g; secobarbital and amobarbital, 100mg and 200mg, depending on subject tolerance, and chlordiazepoxide, 50mg. The administration of hypnotic doses of both barbiturates, secobarbital and amobarbital, significantly accelerated the plasma disappearance and decreased the hypoprothrombinemic effect of warfarin. Neither chlordiazepoxide nor chlorothiazide, administered in standard doses, caused significant alterations in warfarin's action or metabolism. An analysis of variance of the data failed to detect any other effects due to sex, time of year, or sequence of the drugs during the treatment periods. Drugs that can be used safely with warfarin without risk of unpredictable fluctuations in its pharmacologic effect need to be identified. 14 references. (author abstract modified)

64623
AUTHORS: Teehan, Brendan P.; Maher, John F.; Carey, James J. H.; Flynn, Pauline D.; Schreiner, George E.
ADDRESS: Georgetown University Hospital, 3800 Reservoir Road, Washington, D. C. 20007
TITLE: Acute ethchlorvynol (Placidyl) intoxication.
SOURCE: Annals of Internal Medicine.
SOURCEID: 72(6):875-882, 1970.

Experience with 6 consecutive patients with severe acute ethchlorvynol (Placidyl) intoxication is described, and the pertinent literature is reviewed. The typical clinical picture consisted of prolonged deep coma, hypothermia, marked respiratory depression, hypotension that usually responded to conventional therapy, and relative bradycardia despite significant hypotension. Complications included severe infections, cardiorespiratory arrest, peripheral neuropathy, and pulmonary edema. Serum levels were as high as 16.6mg/100ml, and the distribution space exceeded total body water. Clearances by peritoneal dialysis, forced diuresis, and hemodialysis were 18.5, 23, and 64ml/min, respectively. Hourly removal rates ranged from 85 to 210mg/hr by forced diuresis and 175 to 344mg/hr by hemodialysis. The serum half-life was shortened from over 70 hr to 22 hr when hemodialysis was used. 14 references. (author abstract)

64634
AUTHORS: No author.
ADDRESS: Author address not given
TITLE: Blisters from barbiturate poisoning.
SOURCE: Medical World News.
SOURCEID: 11(39):54M, 1970.

Bullous blisters resulting from barbiturate poisoning occur rarely, and may be mistaken for sheet burns in cases of toxic coma. A case is reported of a 55 year old woman who had ingested 30 capsules of Carbrital, made up of 100mg pentobarbital sodium and 260mg of carbromal. The patient was areflexic and her pupils were fixed. Fluid from the blister lesions on the dorsum of her hands, around to knees and on the heels, contained 1.8mg percent barbiturate. The lesions do not appear to be dependent upon the depth of coma or associated complications such as hypotension and respiratory insufficiency, and probably develop from the primary toxic action of the barbiturate on the epidermis. 2 references.

63773
AUTHORS: Simpson, G. M.; Angus, J. W. S.
ADDRESS: Early Clinical Drug Evaluation Unit, Rockland State Hospital, Orangeburg, New York
TITLE: Drug induced extrapyramidal disorders: a rating scale for extrapyramidal side effects.
SOURCE: Acta Psychiatrica Scandinavica (Copenhagen).
SOURCEID: Suppl. 212:11-19, 1970.

A modification of an earlier rating scale devised for extrapyramidal system disturbances is described and evidence is presented for the validity and reliability of the scale. In a double-blind study, patients receiving a placebo were separated from those receiving patent neuroleptic medications (at 2 dose levels). The usefulness of the scale in studies of neuroleptic drugs is discussed. By its application, it is possible to quantify extrapyramidal side-effects and to separate them into 4 principal factors. The scale could be used in routine, early clinical drug evaluation. 9 references. (author abstract modified)

63923
AUTHORS: Finn, Richard.
ADDRESS: Department of Psychiatry, University of Iowa College of Medicine, Iowa City, Iowa
TITLE: Anti-anxiety agents.
SOURCE: Journal of the Iowa Medical Society.
SOURCEID: 60(8):583-584, 1970.

Anti-anxiety drugs can be divided into 2 groups: an older group including barbiturates, chloral hydrate, paraldehyde and ethyl alcohol, and a newer group divided into 3 subgroups: sedating antihistamines (hydroxyzine, promethazine, diphenhydramine), muscle relaxants (mephenesin derivatives and benzodiazepines) and a miscellaneous group of rarely used anti-anxiety agents. Another way to classify anti-anxiety drugs is on the basis of their speed of onset and duration of action. These classifications can help in selecting the best drug for a patient as well as anticipating results of overdosage. Since the sedating antihistamines and the anti-psychotics do not share the cross-tolerance found among barbiturates, muscle relaxants, non-barbiturate hypnotics and ethyl alcohol, they should not be used as the primary replacement agent in treating acute drug withdrawal in patients with a physical dependence to one of the depressants. The newer drugs are now more widely used than all the older drugs; the newer drugs can be titrated to reduce anxiety without producing sedation. Anti-anxiety drugs are apparently most effective in reducing anticipatory anxiety (apprehension). Some specific drug treatments for mental and emotional symptoms now exist and physicians must consider the differential diagnosis of disorders causing such symptoms before prescribing drugs. Tense and anxious patients are difficult to treat. The outcome of treatment depends on a number of nonspecific factors involving the patient, the patient's nontreatment milieu, the type of treatment, the treatment milieu and the doctor. Prescriptions for any of the anti-anxiety drugs should never be open ended; prescriptions should be written only for quantities sufficient to cover the interval between visits. 6 references.

64091
AUTHORS: Scott, George D.
ADDRESS: Institute of Psychotherapy, Kingston, Ontario, Canada
TITLE: Drugs and reality in captive society. Some observations on chemical adaptation.
SOURCE: Canadian Psychiatric Association Journal (Ottawa).
SOURCEID: 15(2):215-222, 1970.

A review of drugs and toxic chemicals found in prisons and of the general prison environment is presented. Prison pharmacology differs from general pharmacology in that drugs with reality relieving side-effects may be searched out by the inmate. Sedative drugs used in prisons are always dangerous and should exclude the pentobarbitals, chloral hydrates and similar drugs which have a transient intoxicating effect. Tranquilizers in usual doses have no realistic effects due to the conditions of penal life. Mood elevators do not improve adjustments because of the let down between doses, and the stimulants should be avoided. Appropriate tension relieving and sleep producing drugs should have no twilight period of intoxication. Drugs advised for use in prisons are phenobarbital, chlorpromazine, levomepromazine, and butyrophenone. A liason with toxic centers in nearby general hospitals should be established with knowledge of available laboratory diagnostic equipment. All toxic chemicals in prison industry should be indexed and recorded at some central point in the institution as to their toxic and antidote characteristics.

64232
AUTHORS: No author.
ADDRESS: Author address not given

TITLE: Lithium carbonate in affective disorders.
SOURCE: Connecticut Medicine.
SOURCEID: 34(3):160, 1970.

Previous reports have shown lithium compounds to be effective when administered prophylactically against recurrent mania and depression. Goodwin's controlled investigation of the effectiveness of lithium salts on these conditions at the National Institute of Health have shown the drug to be effective in improving both mental states. Twelve manic and 18 depressed patients were studied longitudinally on the basis of an initial placebo period, and a period with lithium carbonate followed by 1 or more placebo periods. Some improvement was observed in 40% of the depressed patients, half of whom showed a complete response. Three quarters of the manic patients responded; however, a majority of them showed a rapid onset of relapse within 24 hours following placebo substitution. The criticism that lithium acts only as a weak antidepressant in depressed patients may be due to patient selection. Positive results were observed in those depressed patients with manic-depressive histories. It is hoped that lithium, affecting both electrolyte and biogenic amine metabolism, will have a long range therapeutic value in the treatment of both mania and depression. 3 references.

64272
AUTHORS: Bejerot, Nils.
ADDRESS: Swedish National Medical Research Board, Stockholm, Sweden
TITLE: A comparison of the effects of cocaine and synthetic central stimulants.
SOURCE: British Journal of Addiction (London).
SOURCEID: 65(1):35-37, 1970.

A comparison of the pharmacological effects and symptoms produced by synthetic central stimulants with those produced by cocaine suggest that the relation between the synthetics and the natural product is the same as that between morphine substitutes and morphine. The effects and symptoms from cocaine and the synthetic central stimulants are listed and verifying authors are cited. Because of the mildness of preparation and the wider scope of therapeutic treatment, the risk for toxicomania from the synthetic drugs is less than from cocaine, but the overall effect is the same. 16 references.

64335
AUTHORS: Moravec, Daniel F.
ADDRESS: Author address not given
TRTITLE: /Chloral hydrate in central nervous system depression./
TITLE: A review of pharmacy for nurses.
SOURCE: Hospital Management.
SOURCEID: 109(2):56-57, 1970.

The pharmacology of chloral hydrate is discussed. Chloral hydrate is a principle member of the ethane derivates used in central nervous system depression. Like paraldehyde, chloral hydrate is an irritating substance and when taken by mouth on an empty stomach, it should be well diluted with water or juice, or taken after food followed with water. When ordinarily hypnotic dosages of 500 mg to 1g are given, sedation occurs within 10 to 15 minutes and sleep within an hour. Chloral hydrate is oxidized in the kidney and liver. One of the products found in the urine is urochloric acid which gives a false positive urine sugar test. Habitual use of chloral hydrate results in dependence and addiction and tolerance can increase enormously. The drug is used satisfactorily as a preoperative sedative since it reduces anxiety and induces sleep with little or no respiratory depression.

64484
AUTHORS: No author.
ADDRESS: Author address not given

TRTITLE: /Drug plasma levels in chronic illness./
TITLE: Each to his own therapeutic dosage?
SOURCE: Medical World News.
SOURCEID: 11(30):18-19, 1970.

Drug treatment in chronic illness should include a check for drug plasma levels at the end of the loading period (thus obviating cases of drug failure and toxic side-effects). This was the argument of F. Sjoqvist (from experience with tricyclic antidepressants) and J. R. Gillette (from experience with chlorpromazine and phenylbutazone), of Sweden's Karolinska Institute and the American National Institutes of Health, respectively, at a New York Academy of Sciences conference on Drug Metabolism in Man. Tests have shown individual variations by factors as high as 50. Regimens of nortriptyline (0.2mg/kg t.i.d.) among 39 sets of twins revealed that, among monozygotes, plasma levels were identical, but 5 of 11 pairs of dizygotes differed markedly (up to a factor of 10) in blood levels of the antidepressant. Phenobarbital (known to stimulate hepatic microsomal output of enzymes) administration to one of a set of matching twins was followed by a drop of nortriptyline level to one fourth that of her twin; furthermore, more than 200 such compounds capable of reducing the effectiveness of metabolized drugs have been discovered, including the carcinogenic hydrocarbons and some widely used pesticides. Also discussed at the conference were: a suggested pathway for halogenated hydrocarbon damage to liver; proof of enzyme inhibition status for allopurinol and methylphenidate (using antipyrine as the model drug); and evidence for imipramine as a competitive inhibitor of norepinephrine transport (after release as a transmitter).